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=> d que l35

L1	63839	SEA FILE=WPIDS ABB=ON	PLU=ON	OLIGONUCLEOTID? OR ?OLIGO (2W)
		NUCLEOTIDE OR DNA		
L2	32138	SEA FILE=WPIDS ABB=ON	PLU=ON	L1 (S) (PROTEIN OR ?PEPTIDE?)
L3	1026	SEA FILE=WPIDS ABB=ON	PLU=ON	L2 (S) CONJUGAT?
L6	570	SEA FILE=WPIDS ABB=ON	PLU=ON	L3 AND ?LINK?
L7	10	SEA FILE=WPIDS ABB=ON	PLU=ON	SULFO (2W) (SMCC OR EMCS OR
		GMBS OR KMUS OR MBS OR SIAB OR SMPB OR LS SMPT OR SMPT OR SVSB		
		OR SIACX OR SIA OR SIAXX OR NPJA)		
L8	729	SEA FILE=WPIDS ABB=ON	PLU=ON	(SMCC OR EMCS OR GMBS OR KMUS
		OR MBS OR SIAB OR SMPB OR LS SMPT OR SMPT OR SVSB OR SIACX OR		
		SIA OR SIAXX OR NPJA)		
L9	1	SEA FILE=WPIDS ABB=ON	PLU=ON	L6 AND L7
L10	1	SEA FILE=WPIDS ABB=ON	PLU=ON	L3 AND L7
L11	5	SEA FILE=WPIDS ABB=ON	PLU=ON	L8 AND L3
L12	48973	SEA FILE=WPIDS ABB=ON	PLU=ON	(AMINO OR AMINE) (3A) (GRP# OR
		GROUP#)		
L13	469	SEA FILE=WPIDS ABB=ON	PLU=ON	L1 (S) L12
L14	267	SEA FILE=WPIDS ABB=ON	PLU=ON	L13 AND L2
L15	1	SEA FILE=WPIDS ABB=ON	PLU=ON	L14 AND L8
L16	151	SEA FILE=WPIDS ABB=ON	PLU=ON	L14 AND ?LINK?
L17	6769	SEA FILE=WPIDS ABB=ON	PLU=ON	(THIO### OR SULF###) (3A) (GRP#
		OR GROUP#)		
L18	21	SEA FILE=WPIDS ABB=ON	PLU=ON	L16 AND L17
L19	6	SEA FILE=WPIDS ABB=ON	PLU=ON	L3 AND L18
L20	44	SEA FILE=WPIDS ABB=ON	PLU=ON	L13 AND L3
L21	30	SEA FILE=WPIDS ABB=ON	PLU=ON	L20 AND ?LINK?
L22	6	SEA FILE=WPIDS ABB=ON	PLU=ON	L21 AND L17
L23	6	SEA FILE=WPIDS ABB=ON	PLU=ON	L19 OR L22
L24	10	SEA FILE=WPIDS ABB=ON	PLU=ON	L23 OR L15 OR L11 OR L10 OR L9
L25	26	SEA FILE=WPIDS ABB=ON	PLU=ON	L8 AND L1
L26	6	SEA FILE=WPIDS ABB=ON	PLU=ON	L25 AND CONJUG?
L27	15	SEA FILE=WPIDS ABB=ON	PLU=ON	L25 AND ?LINK?

L28 17 SEA FILE=WPIDS ABB=ON PLU=ON L26 OR L27
 L29 12 SEA FILE=WPIDS ABB=ON PLU=ON L28 NOT L24
 L35 22 SEA FILE=WPIDS ABB=ON PLU=ON L24 OR L29 OR L28

=> d .wp 1-22

L35 ANSWER 1 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 2004-008897 [01] WPIDS
 DNC C2004-002242
 TI New molecular carrier useful for introducing substance e.g.
 pharmacological agent or genetic material into cells, comprising central
 multivalent core to which several adduct molecules are bonded.
 DC A96 B04 B05 B07 D16
 IN CHU, Y L; LAI, W; LI, F Q; QIU, J; ZHU, S
 PA (CHUY-I) CHU Y L; (LAIW-I) LAI W; (LIFQ-I) LI F Q; (QIUJ-I) QIU J;
 (ZHUS-I) ZHU S
 CYC 1
 PI US 2003068379 A1 20030410 (200401)* 30p
 ADT US 2003068379 A1 Provisional US 2001-310492P 20010808, US 2002-137355
 20020503
 PRAI US 2001-310492P 20010808; US 2002-137355 20020503
 AB US2003068379 A UPAB: 20040102
 NOVELTY - A molecular carrier (I) comprising a central multivalent core to
 which several adduct molecules are bonded, is new.
 DETAILED DESCRIPTION - A molecular carrier (I) of formula (F1), (F2)
 and (F3), comprising a central multivalent core to which several adduct
 molecules are bonded, is new.
 Adduct = residue of an amino acid;
 n = integer of 2 or greater;
 m = 0 or a positive integer; and
 p = positive integer.
 INDEPENDENT CLAIMS are also included for the following:
 (1) a pharmacological agent/molecular carrier complex (II) comprising
 (I) and a pharmacological agent that is associated with at least one of
 the adduct moieties;
 (2) a genetic material/molecular carrier complex (III) comprising (I)
 and genetic material which is associated with one of the adduct moieties;
 (3) forming (M1) a molecular carrier by covalently bonding several
 adduct molecules to a central multivalent core molecule by reacting a
 nucleophilic group on each adduct molecule with an electrophilic group on
 the multivalent core molecule, where the multivalent core molecule
 comprises electrophilic groups;
 (4) forming (M2) a molecular carrier comprising covalently bonding
 several adduct molecules to a central multivalent core molecule by
 reacting an electrophilic group on each adduct molecule with a
 nucleophilic group on the multivalent core molecule, where the multivalent
 core molecule comprises nucleophilic groups, and is chosen from
 benzene-tetramine, a tri(carboxymethyl)amine, ((Lys)2Lys)3-(TFA), where
 TFA is a tri-functional amine, diethylaminetriamine, triethylenetetramine,
 Tris(hydroxymethyl)aminomethane (TRIS), and $\text{NH}_2((\text{CH}_2)_n\text{NH})_m(\text{CH}_2)_n\text{NH}_2$,
 where n and m are integers which may vary throughout the molecule;
 (5) a molecular carrier made by (M1) or (M2), and (II) and (III)
 produced by (M1); and
 (6) (II) and (III) comprising a molecular carrier made by (M2).
 USE - (I) is useful for introducing a substance into cells by
 incubating cell(s) with (I) associated with a pharmacological agent (e.g.
 non-peptide drugs, proteins, peptides,
 steroids or hormones) or a genetic material, for in vivo transfection of
 cells, comprising administering (I) associated with a pharmacological

agent or a genetic material, into the cells. (I) is also useful for performing gene therapy by administering a gene therapy agent comprising (I) associated with a genetic material such as an expression vector containing a **DNA** segment encoding a **protein** or an anti-sense **oligonucleotide** to a human or animal. The gene therapy agent (I) is useful for improving the pharmacokinetic profile of a pharmacological agent. (I) may be used to **conjugate** pharmacological agent(s).

ADVANTAGE - (I) provides a drug delivery vehicle that can improve the pharmacokinetics or pharmacological agent.
Dwg.0/15

TECH

UPTX: 20040102

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Molecular Carrier: The molecular carrier is of formula (a).

Preferred Complex: (II) further comprises a second pharmacological agent associated with at least one of the adduct moieties, which is different from the first pharmacological agent. The adduct moiety comprises an enzyme labile bond (preferably a disulfide bond) that is labile to intracellular enzymes, digestive enzymes or serum enzymes. (II) further comprises a receptor, a receptor ligand or a receptor binding **protein** associated with one of the adduct moieties.

The pharmacological agent is chosen from non-**peptide** drugs, **proteins**, **peptides**, steroids and hormones, a **peptide** antigen capable of eliciting an immune response, an opiate **peptide**, a leutinizing hormone releasing hormone (LHRH) antagonist, paclitaxel, or an angiogenic agent which inhibits or stimulates angiogenesis. The molecular carrier comprises maleimide group(s) and the pharmacological agent comprises a **thiol group** and is covalently associated with the molecular carrier by reaction of the **thiol group** on the pharmacological agent with the maleimide group on the molecular carrier.

(II) is dispersed in a solution as an emulsion or suspension, or the molecular carrier is immobilized to a solid support. In (III), the molecular carrier comprises positively charged surface functional group(s), and the genetic material is ionically associated with the molecular carrier through the charged groups. The molecular carrier preferably comprises the residue of a polyfunctional **amine**, where the **amine groups** are protonated to form the charged groups. The genetic material is chosen from **DNA**, RNA, **oligonucleotides**, and nucleic acids. Some of the adduct molecules are bonded to other adduct molecules.

Preferred Method: In (M1), the multivalent core molecule is a polyfunctional-carboxylic acid, succinic acid or ethylene diamine tetraacetic acid (EDTA). The nucleophilic group on each adduct molecule is an **amino group**. The adduct molecules comprise glutamic acid, aspartic acid or its adducts. The adduct molecules preferably comprise tetra-ester of Glu(Glu)₂, octa-ester of (Glu(Glu(Glu)₂)₂), hexadeca-ester of (Glu(Glu(Glu-(Glu)₂)₂)₂) or esters of higher order adducts of glutamic acid. The adduct molecules comprise glutamic acid ester or aspartic acid ester adducts, and the method further comprises a step of hydrolyzing the ester groups on the adduct molecules to the corresponding carboxylic acid groups.

(M1) further comprises:

- (i) reacting a first N-substituted glutamic or aspartic acid with 2 equivalents of a glutamic or aspartic acid di-ester and de-protecting the **amine groups** on the first glutamic or aspartic acid to form a first glutamic or aspartic acid di-ester adduct;
- (ii) optionally reacting a second N-substituted glutamic or aspartic acid with 2 equivalents of first glutamic or aspartic acid di-ester and de-protecting the **amine groups** on the second glutamic

or aspartic acid to form a second glutamic or aspartic acid di-ester adduct;

(iii) optionally reacting a third N-substituted glutamic or aspartic acid with 2 equivalents of the second glutamic or aspartic acid di-ester adduct and de-protecting the **amine group** on the third glutamic or aspartic acid to form a third glutamic or aspartic acid di-ester adduct; and

where the adduct molecules covalently bonded to the multivalent core comprise the first, second and/or third glutamic or aspartic acid di-ester adducts. The adduct molecules comprise enzyme labile **linkages**, preferably disulfide **linkages**.

(M1) further comprises a step of associating a pharmacological agent with the molecular carrier, by covalently bonding the agent to the carrier. The step also involves associating a receptor or a receptor ligand with the carrier. The reacting step is conducted in the presence of a catalyst e.g. carbodiimide, preferably 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC) or N,N-dicyclohexyl-carbodiimide (DCC). The molecular carrier comprises carboxylic acid surface functional groups, and the method further involves:

(a) reacting surface functional carboxylic acid group(s) on the molecular carrier with a polyamine to provide **amine** surface functional **groups**, and ionically complexing genetic material to the **amine** surface functional **groups**; or

(b) reacting a compound comprising a maleimide group and a carboxylic acid reactive functional group with the surface functional group(s) to provide maleimide surface functional group(s), and covalently attaching a pharmacological agent to the molecular carrier by reacting a **thiol group** on the pharmacological agent with the maleimide group(s) on the molecular carrier.

The pharmacological agent is preferably a **peptide** containing a cysteine residue. The core molecule is chosen from benzene-tetracarboxylic acid, cyclopentane-tetracarboxylic acid, butane-tetracarboxylic acid, ethylenediamine tetralkylcarboxylic acid, ethylene glycol-bis(beta-amino-ethyl ether)-N,N,N',N'-tetraacetic acid, 1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid, spermidine pentaacetic acid, spermine-hexaacetic acid, ((COOH)CH₂)₂ N(CH₂)₃ NCH₂COOH(CH₂)₃ NH₂, and (COOH)CH₂)₂ N(CH₂)₃ NCH₂ COOH(CH₂)₂ NH₂.

In (M2), the adduct molecules comprise lysine or arginine residues, and the method further comprises:

(i) reacting a first lysine or arginine ester molecule with 2 equivalents of lysine or arginine and hydrolyzing the ester group on the first lysine or arginine to a carboxylic acid to form a first lysine or arginine adduct;

(ii) optionally reacting a second lysine or arginine ester with 2 equivalents of the first lysine or arginine adduct and hydrolyzing the ester group on the second lysine or arginine ester to a carboxylic acid to form a second lysine or arginine adduct;

(iii) optionally reacting a third lysine or arginine ester with 2 equivalents of the second lysine or arginine adduct and hydrolyzing the ester group on the third lysine or arginine ester to a carboxylic acid to form a third lysine or arginine adduct; and

where the adduct molecules covalently bonded to the multivalent core comprise the first, second and/or third lysine or arginine adducts.

L35 ANSWER 2 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2003-697456 [66] WPIDS

CR 1997-332441 [30]

DNC C2003-191750

TI New homogeneous prodrug **conjugate** containing hepatic ligand for delivery of pathogen-specific oligomer useful for treating liver

infections or cancer.

DC B04 C03 D16
 IN DEAMOND, S; DUFF, R; ROBY, C; TS'O, P O P; ZHOU, Y
 PA (CELL-N) CELL WORKS INC; (UYJO) UNIV JOHNS HOPKINS
 CYC 100
 PI WO 2003067209 A2 20030814 (200366)* EN 107p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZM ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
 RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
 ZW

ADT WO 2003067209 A2 WO 2002-US19908 20020621

PRAI US 2001-888164 20010622

AB WO2003067209 A UPAB: 20031014

NOVELTY - Homogeneous **conjugate** (I) comprising a hepatic ligand, bifunctional **linker** and biologically stable oligomer that binds to a sequence in a hepatic virus or pathogen and is released from the **conjugate** by hydrolysis or reduction, is new.

DETAILED DESCRIPTION - Homogeneous **conjugate** of formula A-L-P (I) comprising a hepatic ligand that specifically binds to a hepatic receptor; bifunctional **linker** that is covalently **linked** to the hepatic ligand and biologically stable oligomer that binds to an (encapsidation) sequence in a hepatic virus or pathogen and is released from the **conjugate** by hydrolysis or reduction of biochemical **linkage(s)** and contains internucleotide **linkages** resistant to enzymatic hydrolysis or biodegradation upon release from the **conjugate**.

A = hepatic ligand, specific for a hepatic receptor that facilitates entry of (I) into receptor-bearing cells;

L = bifunctional **linker** covalently **linked** to A and P in regiospecific manner; and

P = biologically stable oligomer that binds to an encapsidation sequence of a hepatic virus.

P is released from the **conjugate** following hydrolysis or reduction of at least one specific biochemical **linkage**. It contains internucleotide **linkages** resistant to enzymatic hydrolysis or biodegradation on release from the **conjugate**.

An INDEPENDENT CLAIM is also included for synthesis and radiolabeling of (I), where the oligomer is an **oligonucleotide**, analog, or oligonucleoside.

ACTIVITY - Virucide; Hepatotropic; Antiinflammatory; Cytostatic; Antiparasitic.

When 10 micro M of the **conjugate** (Ia) was administered to confluent monolayers of HepG2 2.2.15 cells, the amount of hepatitis B virions (pg/106 cells) formed was only about 200; compared to about 1400 in the absence of (Ia).

Tyr-Glu-Glu-(ahGalNAc)-3-**SMCC**-5'-AAAGCCACCCAAGGCA (Ia)

SMCC = hydroxysuccinimidyl-4-(N-methylmaleimido)cyclohexyl carboxylate;

MECHANISM OF ACTION - Antisense inhibition of protein synthesis. No biological data given.

USE - (I) are used as prodrugs for delivering therapeutic oligomers to liver cells, for treatment, in human or veterinary medicine, of viral or parasitic diseases or hepatic cancer, most especially infection by hepatitis B, C or D viruses.

ADVANTAGE - The A-L component provides ligand-directed, receptor-mediated deliver of (I) to hepatocytes, where the active agent (P) is released.

Dwg.0/20

TECH

UPTX: 20031014

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Materials: The oligomer is an **oligonucleotide** or analog, or oligonucleoside that targets a hepatitis virus and binds to an RNA sequence in the preS1 open reading frame. Particularly it includes deoxyribose methylphosphonate, phosphorothioate or phosphodiester internucleotide **linkages**, optionally also 2'-O-methyl ribose residues, or any combination of them. Three **oligonucleotide** sequences are specified, most preferred is S3 which targets the unpaired loop of the encapsidation site of the hepatitis B virus pregenome.

AAAGCCACCCAAGGCA (S3)

The most preferred **conjugate** is Tyr-Glu-Glu-(ahGalNAc)-3-

SMCC-5'-AAAGCCACCCAAGGCA

SMCC = hydroxysuccinimidyl-4-(N-methylmaleimido)cyclohexyl carboxylate.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation (claimed): Synthesizing the **conjugate** comprises:

- (a) forming an A-L construct;
- (b) purifying the A-L construct to over 95 % homogeneity and removing any unreacted L;
- (c) modifying P to form a thiol-modified oligomer;
- (d) purifying the thiol-modified oligomer under degassed conditions;
- (e) reacting the A-L construct and the thiol oligomer in a two-component **conjugation** reaction under degassed conditions, where the reaction is performed using excess amounts of the ligand scaffold or the thiol modified oligomer to form the A-L -P **conjugate**; and
- (f) purifying the A-L-P **conjugate** by size-exclusion chromatography (SEC).

Alternatively, L, with a terminal disulfide residue, is attached to P during its solid-phase synthesis, the product is purified, reduced to thiol and then reacted with A. In this case, A-L-P is purified by electrophoresis or HPLC and the modified oligomer is purified by SEC.

A typical process for radiolabeling the **conjugate** is:

- (a) adding the tracer unit 5'-T-3'-ps-3'-T-ps-T-5' to the 3'-end of P, during synthesis;
- (b) enzymatic phosphorylation to incorporate radiolabeled phosphate (using polynucleotide kinase and labeled adenosine triphosphate); and
- (c) chemically modifying the radioactive phosphate by **conjugation** to an amine, to protect it against enzymatic degradation.

Alternatively, radiolabeling the **conjugate** comprises:

- (a) adding a disulfide-terminated **linker** to the 5' end of P and adding the tracer unit 5'-T-3'-ps-3'-T-ps-T-5' to the 3'-end of P, during synthesis;
- (b) purifying the disulfide and tracer containing P;
- (c) reducing the disulfide functional group to a thiol group to form a thiol modified P;
- (d) purifying the thiol-modified P using SEC to remove unreacted reagent;
- (e) **conjugating** an A-L construct to the purified thiol-modified P;
- (f) enzymatically phosphorylating the tracer unit to incorporate radiolabeled phosphate (using polynucleotide kinase and labeled adenosine triphosphate); and
- (g) chemically modifying the radioactive phosphate by **conjugation** to an amine, to protect it against enzymatic degradation.

L35 ANSWER 3 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2003-568888 [53] WPIDS

DNN N2003-452509 DNC C2003-153306

TI Detection of an enzyme useful in drug discovery involves measuring a

change in deflection of a microcantilever having a substrate for the enzyme.

DC A89 B04 D16 P42 S03
 IN BOTTOMLEY, L A; GHOSH, M; SAUL, R; SHEN, S
 PA (PROT-N) PROTIVERIS INC
 CYC 100
 PI WO 2003023363 A2 20030320 (200353)* EN 16p
 RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
 MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
 RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
 ZW
 US 2003068655 A1 20030410 (200353)
 ADT WO 2003023363 A2 WO 2002-US28920 20020911; US 2003068655 A1 US 2001-951131
 20010912
 PRAI US 2001-951131 20010912
 AB WO2003023363 A UPAB: 20030820

NOVELTY - Detecting (M1) an enzyme by:
 (a) depositing a coating material (c1) on a first surface of at least one microcantilever (m1);
 (b) adding at least one substrate (s1) (capable of interacting with the enzyme or the substance) to (c1);
 (c) exposing (m1) with (s1) to a sample; and
 (d) measuring a deflection of (m1), where the deflection indicates a presence of the enzyme in the sample, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) detection (M1') of an associating substance in a sample, where the substance binds to (s1) and the detection involves at least one (m1) configured to be responsive to a micro-force, involving steps (1), (2), exposing (m1) with (s1) to the sample, and measuring a resulting free surface energy change, where the energy change indicates binding to (s1) by the associating substance in the sample;
 (2) a method (M2) of screening for an inhibitor of an enzyme having (s1) on (m1) having a coating involving:
 (a) adding (s1) (which is capable of interacting with the enzyme) to a first side of a first (m1) and a second (m1);
 (b) exposing the first (m1) with (s1) to a sample containing a candidate inhibitor and the enzyme; and
 (c) measuring a deflection of the first (m1) in comparison to a deflection of the second (m1) identically exposed to the enzyme and in the absence of the candidate inhibitor; and
 (3) an apparatus to measure a micro-force generated by an interaction between the enzyme and a bio-material (preferably enzymatic substrate or enzymatic pseudo-substrate), comprising at least one (m1), a coating material deposited on a first surface of (m1), a bio-material attached to the coating material and at least one interaction cell containing (m1) housed in a micro-fluidics device for receiving a sample, where the detection of the micro-force is indicated by deflection of (m1) due to the presence of the enzyme in the sample.

USE - For detecting an enzyme associated with a medical condition (e.g. genetic defect, Fabry disease, Gaucher disease, Tay-Sachs disease, Lesch-Nyhan disease, mannosidosis disease, X-linked glomerular disease and mucopolysaccharidosis, cancer (e.g. brain, liver, pancreas, lung, prostate, and breast) in a vertebrate animal; the presence of infectious agent e.g. virus, bacterium, fungus, protozoan and helminth) (all claimed). Also useful in proteomics, drug discovery, medical research, medical, veterinary, dental diagnostics, forensics and military

applications, in research; for detection and analysis of binding activities of enzymes and enzyme-like proteins.

ADVANTAGE - The methods detect the interaction between enzymes and their substrates.

Dwg.0/4

TECH

UPTX: 20030820

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Step (b) of M1 involves adding at least one biomaterial or a drug; and designing (m1) for detecting the enzyme. The deflection is caused by a change in stress on the surface of (m1).

Preferred Enzyme: The enzyme is hydrolase (preferably protease), oxidoreductase, transferase, lyase, ligase, kinase, phosphatase, endopeptidase, exopeptidase, restriction endonuclease, exonuclease or polymerase, or a component (c2). The protease is a metalloprotease or serine protease. The transferase is glycosyl transferase, glutathione S-transferase, an acetyl transferase or a DNA methyl transferase. The lyase is polysaccharide lyase, a 3-hydroxy-3-methylglutaryl Coenzyme A lyase, argininosuccinate lyase or an isocitrate lyase. The oxidoreductase is hydroxylamine oxidoreductase, glyphosphate oxidoreductase, quinine oxidoreductase, ubiquinone oxidoreductase or a protein disulfide oxidoreductase. When present in the sample, the enzyme is substantially purified. (c2) is prostate specific antigen or collagenase.

Preferred Components: In (M1'), the associating substance is an enzyme, which binds (s1) and fails to dissociate, and has no activity on (s1). In (M1'), (s1) is a non-cleavable pseudo-substrate, several bio-materials or an inhibitor of enzymatic activity. In the apparatus, the bio-material comprises an enzymatic pseudo-substrate.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Method: In step 4), the deflection is measured by optical, electron tunneling, capacitive, piezoelectric or piezoresistive methods (preferably by optical method including a laser). The method (M1) further involves analyzing the deflection of (m1) as a function of a time parameter determined from the time of exposing (m1) to the sample by using a microprocessor; prior to adding (s1) to the first surface, reacting the first surface with a bifunctional cross-linker, where the bifunctional cross-linker is capable of further reacting with (s1). The microprocessor compares, calculates and stores the deflection of (m1) as a function of the time parameter. The analyzing step additionally involves analyzing a parameter selected from concentration of enzyme, concentration of substrate, presence of a cofactor and presence of an inhibitor.

Preferred Apparatus: (m1) has a length of about 100 - 750 microm, width of 20 - 300 microm and thickness of 0.1 - 10 microm. In (M2), the first (m1) is located in a first interaction cell and the second (m1) is located in a second interaction cell of a micro-fluidics device. A third (m1) is located in a third interaction cell and a fourth (m1) is located in a fourth interaction cell, which are exposed to a different concentration of enzyme than the first and second cells; or different samples containing candidate inhibitors than the candidate in the first interaction cell. In (M1), (m1) is in a block array containing several (m1). The apparatus is disposable and reusable.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The biofunctional cross-linker is dithiobis(succinimido undecanoate (DSU), long chain succinimido-6-(3-(2-pyridyldithio)-propionamido)hexanoate (LCSPDP), succinimidyl-6-(3-(2-pyridyldithio)-propionamido)hexanoate (SPDP), or m-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS) (preferably (DSU)).

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: In (M1), the substance is a nucleic acid, protein, lipid, hydrocarbon or a polysaccharide. In (M1), the sample is a biological fluid selected from cell lysate, culture medium, spent medium, animal extract, plant extract; bodily fluid from a vertebrate animal (preferably mammal e.g. human). The bodily fluid is blood, lymph, tissue fluid, urine, bile, sweat, synovial fluid, amniotic fluid, abdominal fluid, pericardial fluid, pleural fluid, cerebrospinal fluid, gastric juice, intestinal juice, joint cavity fluid, tears or nasal discharge. In (M1'), the associating substance is a binding protein, cofactor, receptor ligand, antibody, polysaccharide, lipid, nucleic acid or steroid.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Method: In M1, step (a) further involves depositing metal(s), where a first layer of chromium and a second layer of gold, or a first layer of titanium and second layer of gold is deposited.

Preferred Metal: The metal is amalgam, an alloy; or a component (c1). (c1) is aluminum, copper, gold, chromium, titanium or silver (preferably gold). (m1) has a second surface selected from aluminum oxide, iridium oxide, silicon, silicon oxide, silicon nitride, tantalum pentaoxide or plastic polymer. In the apparatus, the second surface of (m1) is silicon, silicon nitride, other silicon compounds, metal compounds, gallium arsenide, germanium, germanium dioxide, glass, zinc oxide, diamond, quartz, palladium or plastic polymer. In the apparatus, the coating material is (c1).

L35 ANSWER 4 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 2003-543481 [52] WPIDS
 DNC C2003-147566
 TI New hybridization substrate for use in a complementarity test, comprises **DNA** strands having a double-strand portion and a single-strand portion, that are immobilized on the surface of a substrate.
 DC B04 D16
 IN HARA, M; ITO, E; NAKAJIMA, K; NAKAMURA, F
 PA (RIKE) RIKEN KK; (HARA-I) HARA M; (ITOE-I) ITO E; (NAKA-I) NAKAJIMA K; (NAKA-I) NAKAMURA F
 CYC 32
 PI EP 1279434 A2 20030129 (200352)* EN 10p
 R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC
 MK NL PT RO SE SI SK TR
 JP 2003043037 A 20030213 (200352) 9p
 US 2003022227 A1 20030130 (200352)
 ADT EP 1279434 A2 EP 2002-16613 20020725; JP 2003043037 A JP 2001-228374 20010727; US 2003022227 A1 US 2002-205363 20020726
 PRAI JP 2001-228374 20010727
 AB EP 1279434 A UPAB: 20030813
 NOVELTY - A hybridization substrate (I), comprises **DNA** strands having a double-strand and single-strand portion immobilized on a substrate surface, where the double-strand portion of the **DNA** strands is immobilized on the substrate surface.
 DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the manufacture (M) of (I), comprising contacting **DNA** strands having a double-strand and single-strand portion, and a thiol group present on the terminal of the double-strand portion, with the metal surface of a metal substrate or a substrate having a metal coating, to immobilize the **DNA** strands on the metal surface.
 USE - (I) Is useful in a complementarity test, in which target **DNA** is contacted with the surface of (I) on which **DNA** strands have been immobilized to test for complementarity between the target **DNA** and the single-strand portion of the **DNA**

strands having a double-strand portion and a single-strand portion. The presence or absence of hybridization between the target **DNA** and the single-strand portion of the **DNA** strands is detected by a surface plasmon resonance method or quartz crystal microbalance (QCM) method. The target **DNA** is a **DNA** having a fluorescent label and hybridization with the single-strand portion of the **DNA** strand is detected using fluorescence or a radioisotope (RI), and target **DNA** comprising a mismatched nucleic acid base is also detected (claimed).

ADVANTAGE - (I) Is cost-effective.

DESCRIPTION OF DRAWING(S) - The figure shows the scheme of preparing thiolated **DNA** oligomer, and the hybridization process.
Dwg.1/4

TECH

UPTX: 20030813

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Substrate: The substrate is a metal substrate or a substrate having a metal coating, or a glass or silicon substrate, and the **DNA** strands have been immobilized on the metal surface of the substrate, using a sulfur atom. The number of nucleic acids of the double-strand and single-strand portion ranges from 10 - 80 and 20 - 90, respectively. In addition to the **DNA** strands having a double-stranded and a single-stranded portion, **DNA** strands having only a double-strand portion have been further immobilized on the surface of the substrate. The immobilization ratio of the **DNA** strands having a double- and single-strand portion, to **DNA** strands having only a double-strand portion ranges from 99:1 - 1:99. The metal substrate or metal coating is made of gold. Preferred Method: The surface of a glass or silicon substrate is surface treated with a hetero bifunctional **crosslinking** agent to immobilize the **DNA** strands on the surface. Contacting with the **DNA** strands is conducted in the presence of bivalent ions e.g. magnesium ions. The hetero bifunctional **crosslinking** agent is selected from succinimidyl-4-(maleimidophenyl)butyrate (**SMPB**), m-maleimidobenzoyl-N-hydroxysuccinimidoester (**MBS**), succinimidyl-4-(maleimidomethyl)cyclohexane-1-carboxylate (**SMCC**), N-(gamma-maleimidobutyloxy)succinimidoester (**GMBS**), m-maleimidopropionic acid-N-hydroxysuccinimidoester (**MPS**), and N-succinimidyl(4-iodoacetyl)amino benzoate (**SIAB**).

L35 ANSWER 5 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2003-441258 [41] WPIDS

DNC C2003-116747

TI Producing **oligonucleotide-protein conjugate** by contacting **oligonucleotide** having **amino group** with **linker** having two **groups** reactive with **amino** and **thiol groups**, contacting **conjugate** formed with **protein** having **thiol group**.

DC B04 D16

IN FAROOQUI, F; REDDY, P M

PA (FARO-I) FAROOQUI F; (REDD-I) REDDY P M; (BECI) BECKMAN COULTER INC

CYC 28

PI WO 2003035830 A2 20030501 (200341)* EN 32p

RW: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK
TR

W: AU CA CN DE GB JP

US 2003092901 A1 20030515 (200341)

ADT WO 2003035830 A2 WO 2002-US32317 20021011; US 2003092901 A1 US 2001-32592
20011024

PRAI US 2001-32592 20011024

AB WO2003035830 A UPAB: 20030630

this option

NOVELTY - Producing (M) **oligonucleotide-protein conjugate** (C1), comprising contacting **oligonucleotide** having an **amino group** (AG) with a heterofunctional **linker** (HL) having first group (G1) reactive with AG and second group (G2) reactive with **thiol group** (TG), where G1 becomes bonded to AG to form **oligonucleotide-HL conjugate** (C2), and contacting (C2) with **protein** having TG, where TG becomes bonded to G2 to form C1, is new.

DETAILED DESCRIPTION - Producing (M) an **oligonucleotide-protein conjugate**, involves contacting an **oligonucleotide** having an **amino group** with a heterofunctional **linker**, where the **linker** has a first group reactive with the **amino group** and a second group reactive with a **thiol group**, where the contacting is performed under conditions sufficient to permit the first group of the **linker** to become bonded to the **amino group** of the **oligonucleotide**, to form an **oligonucleotide-heterofunctional linker conjugate**, and contacting the **oligonucleotide-heterofunctional linker conjugate** with a **protein** having a **thiol group** reactive with the second group of the **linker**, where the contacting is performed under conditions sufficient to permit the **thiol group** of the **protein** to become bonded to the second group of the **linker** of the **oligonucleotide-heterofunctional linker conjugate**, to form the **oligonucleotide-protein conjugate**.

An INDEPENDENT CLAIM is also included for an **oligonucleotide-protein conjugate** produced by (M).

USE - (M) is useful for producing an **oligonucleotide-protein conjugate**. (I) is useful for determining the presence or concentration of a target nucleic acid molecule (preferably a nucleic acid molecule of a pathogen or a tumor cell) in a sample, by contacting the sample with (I), where a sequence of an **oligonucleotide** portion of (I) is selected to be able to hybridize with the target nucleic acid molecule, and detecting a **protein** portion of any of (I) having an **oligonucleotide** portion hybridized to the target nucleic acid molecule, where the detection determines the presence or concentration of the target nucleic acid molecule in the sample. (I) is useful for determining the presence or concentration of a target analyte in a sample, by contacting the sample with (I), where a **protein** portion of (I) is selected to be able to bind to the target analyte, and detecting an **oligonucleotide** portion of any of (I) having a **protein** portion bound to the target analyte, where the detection determines the presence or concentration of the target analyte in the sample (all claimed). (I) is useful for detecting the presence or absence of a nucleic acid sought to be detected in a biological medium, which may contain other nucleic acids that are not sought, or to assay for the presence of binding ligands to the **conjugated protein**, and the presence of concentration of such ligands.

Dwg.0/2

TECH

UPTX: 20030630

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (M), the **amino group** is at the 3' or 5' end of the **oligonucleotide**. The step of contacting the **oligonucleotide** with the **linker** additionally comprises forming the **oligonucleotide** having the 3' or 5' **amino group**. The **oligonucleotide** having the 3' **amino group** is formed by synthesizing the **oligonucleotide** on a

3'-amino CPG solid support. The **amino group** is at an internal site of the **oligonucleotide**. The step of contacting the **oligonucleotide** with the **linker** additionally comprises forming the **oligonucleotide** having the internal **amino group**. The modified **amino group** is C7 CPG. The first group of the heterofunctional **linker** is an NHS group, and the second group is a maleimide group. The heterofunctional **linker** is selected from sulfosuccinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (**sulfo-SMCC**), N-(epsilon-maleimidocaproyloxy)sulfosuccinimide ester (**sulfo-EMCS**), N-(gamma-maleimidobutyryloxy)sulfosuccinimide ester (**sulfo-GMBS**), N-(K-maleimidoundecanecanoyloxy)sulfosuccinimide ester (**sulfo-KMUS**), m-maleimidobenzoyl-N-hydroxysulfosuccinimide ester (**sulfo-MBS**), sulfosuccinimidyl(4-iodoacetyl)aminobenzoate (**sulfo-SIAB**), sulfosuccinimidyl 4-(p-maleimidophenyl)butyrate (**sulfo-SMPB**), sulfosuccinimidyl-6-(alpha-methyl-alpha-(2-pyridyldithio)toluamido) hexanoate (**sulfo-LC-SMPT**), N-succinimidyl-4-vinylsulfonylbenzoate (**SVSB**), succinimidyl 6-(4-iodoacetyl)amino methyl-cyclohexane-1-carbonyl)amino hexanoate (**SIACX**), N-succinimidyl iodoacetate or iodoacetic acid N-hydroxysuccinimide ester (**SIA**), succinimidyl 6(6-(((iodoacetyl)amino hexanoyl)aminohexanoate)) (**SIAXX**) and p-nitrophenyl iodoacetate (**NPIA**). The **thiol group** of the **protein** is derived from an iminothiolane moiety. The step of contacting the **oligonucleotide** -heterofunctional **linker conjugate** with a **protein** having a **thiol group**, additionally comprises forming the **protein** having the **thiol group**. The **protein** is formed by reacting the **amino group** of a **protein** with iminothiolane. The **protein** is an enzyme (selected from alkaline phosphatase, beta-galactosidase, horse radish peroxidase and urease), hapten, immunoglobulin (preferably an immunoglobulin that is able to bind to a drug, a receptor, a receptor ligand, a tumor antigen, or an antigen that is characteristic of a pathogen), streptavidin, avidin or phycobillin **protein**.

L35 ANSWER 6 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 2002-713479 [77] WPIDS
 DNC C2002-202313
 TI New composition, useful as vaccine against bacterial, viral, parasitic or fungal infections, or cancer, in animals and humans, comprises M cell-specific ligand, nucleic acid encoding an immunogen, and a nucleic acid binding moiety.
 DC B04 C06 D16
 IN PASUAL, D W
 PA (RERE-N) RES & DEV INST INC
 CYC 100
 PI WO 2002072015 A2 20020919 (200277)* EN 102p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZM ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
 RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
 ZW
 ADT WO 2002072015 A2 WO 2002-US7254 20020312
 PRAI US 2001-274639P 20010312
 AB WO 200272015 A UPAB: 20021129

NOVELTY - A composition comprising an M cell-specific ligand, a nucleic acid sequence encoding an immunogen, and a nucleic acid binding moiety, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a vaccine comprising the composition and an excipient;
- (2) a method for immunizing a host against an immunogen by administering the vaccine to the host;
- (3) a method for assaying for mucosal immunity, comprising:
 - (a) administering the vaccine to an animal which is free of infection from the infectious agent whose antigen is to be tested;
 - (b) isolating mucosal immune cells from the animal; and
 - (c) co-incubating the isolated cells with heterologous antigen expressing or presenting cells, where lysing of antigen expressing cells is indicative of mucosal immunity in the animal;
- (4) an isolated nucleic acid encoding a fusion protein comprising a nucleic acid binding moiety and an M cell-specific ligand;
- (5) a vector comprising the nucleic acid;
- (6) an isolated polypeptide comprising the expression product of the vector, or a nucleic acid binding moiety and an M cell-specific ligand;
- (7) a host cell comprising the vector;
- (8) a method of expressing a fusion protein, comprising the step of expressing the vector;
- (9) an isolated antibody that binds to the polypeptide;
- (10) a kit comprising an M cell-specific ligand and a nucleic acid or immunogen binding moiety; and
- (11) a pharmaceutical composition formulated for mucosal delivery comprising an M cell-specific ligand and an immunogen.

ACTIVITY - Immunomodulator; Antibacterial; Virucide; Antiparasitic; Antifungal; Cytostatic. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The composition is useful as a vaccine to induce an immune response against the immunogen or against the disease with which the immunogen is associated (claimed). The kit is useful in delivering a nucleic acid vaccine or other vaccine to mucosal lymphoid tissue, and for measuring a mucosal immune response raised against the nucleic acid vaccine or other vaccine (claimed). The methods are useful for immunizing animals and human subjects against bacterial, viral, parasitic, fungal infectious agents or cancer.

Dwg.0/7

TECH

UPTX: 20021129

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Composition: The composition comprises a nucleic acid sequence that is, specifically, a **DNA** sequence. The nucleic acid binding moiety is a **polypeptide** comprising a polymeric chain of basic amino acid residues, such as polylysine. The **polypeptide** is a fusion **protein** further comprising the M cell-specific ligand. The immunogen is selected from immunogens expressed by infectious agents and tumor specific antigens. The infectious agent may be a bacterium, parasite, fungus, virus or a prion, such as tuberculo bacillus, leprosy bacillus, malaria parasite, diphtheria bacillus, tetanus bacillus, Leishmania, Salmonella, Schistosoma, measles virus, mumps virus, herpes virus, HIV, cancer or influenza virus. The M cell-specific ligand comprises the **protein** 1 of a reovirus or its tetramer or primer, adhesin derived from Salmonella, adhesin derived from polio virus or M cell tropic fragments. The **DNA** sequence further comprises a plasmid vector in which the **DNA** sequence encoding an immunogen is operably **linked** to transcription regulatory elements. The above composition further comprises a **linker**, which is a **crosslinker**, and an M cell-specific ligand **conjugated** to an immunogen that is

encapsulated or surface-displayed in a liposome. The **crosslinker**, which is a complexing moiety, consists of SPDP, DSS, **SIAB**, **SATA**, **MBS** or **GMBS** (undefined). The complexing moiety comprises nitrilotriacetic (NTA)-metal complex and iminodiacetic acid (IDA)-metal. The M cell-specific ligand and the immunogen are **conjugated** or are comprised in a fusion **protein** or **polypeptide**.

Preferred Vaccine: The vaccine, which is a therapeutic vaccine, induces a protective immune response in a vaccinated host against the immunogen. The vaccine further comprises an adjuvant consisting of an immunomodulator. The immunomodulator comprises cytokines, lymphokines, interleukins, interferons or growth factors. The vaccine, which is formulated in unit dosage form, is further packaged with instructions for use.

Preferred Method: In assaying for mucosal immunity, the mucosal immune cells are isolated from tissues selected from lamina propria tissue, intraepithelial tissue, Peyer's patches, lymph nodes, nasal passages, NALT, adenoids, and vaginal epithelium. This method further comprises the step of evaluating the animal's cytokine profile.

Preferred Vector: The vector, which is an expression vector, comprises a nucleic acid that is in operable **linkage** consisting of sense and antisense orientations relative to transcriptional elements comprising the vector.

Preferred Kit: The kit further comprises instructions for its use.

L35 ANSWER 7 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 2002-373742 [41] WPIDS
 DNC C2002-105869
 TI A single chain insulin analog (**SIA**) compound used in the treatment of type I diabetes, comprises the properties of greater insulin receptor binding activity than proinsulin and less insulin receptor binding activity than insulin.
 DC B04 D16
 IN KIM, K; KIM, S; LEE, H C; SHIN, H; YOON, J; KIM, G S; KIM, S J; SHIN, H C; KIM, K S
 PA (LEE-H-I) LEE H C; (KIM-K-I) KIM K S; (KIM-S-I) KIM S; (SHIN-H-I) SHIN H; (YOON-I) YOON J
 CYC 29
 PI EP 1193272 A1 20020403 (200241)* EN 24p
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
 KR 2002026756 A 20020412 (200267)
 JP 2002320490 A 20021105 (200304) 19p
 US 6630348 B1 20031007 (200374)
 ADT EP 1193272 A1 EP 2001-121651 20010913; KR 2002026756 A KR 2000-58003 20001002; JP 2002320490 A JP 2001-306269 20011002; US 6630348 B1 US 2000-706690 20001107
 PRAI US 2000-706690 20001107; KR 2000-58003 20001002
 AB EP 1193272 A UPAB: 20020701
 NOVELTY - A single-chain insulin analog (**SIA**) compound (I) comprising the properties of greater insulin receptor binding activity than proinsulin and less insulin receptor binding activity than insulin, is new.
 DETAILED DESCRIPTION - A single-chain insulin analog compound (I) comprises the properties of greater insulin receptor binding activity than proinsulin and less insulin receptor binding activity than insulin. (I) has the formula:
 B chain - X - A chain (I);
 B and A = human insulin chains or functional analogs; and
 X = a joining peptide of 5 to 18 amino acids.
 INDEPENDENT CLAIMS are also included for the following:

- (1) a polynucleotide encoding (I);
- (2) a recombinant vector comprising the polynucleotide;
- (3) a cell line transformed with the vector;
- (4) treating (M1) a patient suffering from diabetes comprises:
 - (a) generating a recombinant viral or plasmid vector comprising a polynucleotide encoding a single-chain insulin analog operatively **linked** to a promoter; and
 - (b) introducing the recombinant viral or plasmid vector to patient, so that expression of polynucleotide results in remission of diabetes;
- (5) treating (M2) a patient suffering from diabetes comprises administering (I) to a patient.

ACTIVITY - Antidiabetic.

rAAV-LPK-SIA (recombinant adeno-associated virus-L-type pyruvate kinase gene promoter-single-chain insulin analog) was administered into diabetic NOD mice by intraportal injection and monitored the blood glucose levels. The blood glucose levels gradually decreased in the rAAV-LPK-SIA-treated NOD mice (10 virus particles), reached the level of normoglycemia at 7 days after treatment, and remained in a normoglycemic state for more than 5 months. In contrast, diabetic NOD mice treated with rAAV-SIA (without the LPK promoter) remained hyperglycemic and died within 3 weeks. When the presence of the SIA gene in the hepatocytes of NOD mice were examined at 15 weeks after treatment with rAAV-LPK-SIA, it was discovered that SIA DNA was integrated into the chromosomal DNA. SIA expression was then examined in the liver and plasma of the mice after glucose loading at 5, 10, and 15 weeks after treatment with rAAV-LPK-SIA, and found that SIA mRNA was clearly expressed and SIA protein was released in the plasma. Anti-SIA antibody was not detected in the sera from these mice during the 5 months after treatment.

MECHANISM OF ACTION - Single-chain insulin analog (claimed); Gene therapy.

USE - (I) is used to treat type I diabetes mellitus (claimed).
Dwg.0/4

TECH

UPTX: 20020701

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Compound: X is preferably 6-9 amino acids and has the formula:

U1-Zn-Ym-Z1-Un;

U = arginine or lysine residue;

Z = amino acid residue;

Y = a peptide;

1 = an integer of 2-n;

n = an integer of 0, 1 or 2; and

m = an integer of 2 to 5.

Preferably, Z is glycine and Y is gly-pro-gly, ala-pro-gly-asp-val, tyr-pro-gly-asp-val or his-pro-gly-asp-val.

Preferred Vector: The vector may be a plasmid or a virus such as an adeno-associated virus. Preferably the vector comprises an inducible promoter, regulated by glucose, such as pyruvate kinase gene promoter, or preferably, a hepatocyte-specific L-type pyruvate kinase gene promoter.

Preferred Method: The viral vector in (M1) is an adeno-associated virus comprising an inducible promoter, regulated by glucose. In the treatment of diabetes, the diabetes is type I diabetes and the vector is introduced to the patient through the cell line which is transformed with the vector.

Preparation: (I) is prepared by standard genetic recombinant techniques.

L35 ANSWER 8 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2002-268789 [31] WPIDS

DNC C2002-079652

TI Gene-delivery compound for targeted gene delivery, comprises single-chain

binding polypeptide having effector segment with cysteinyl residue and nucleic acid-binding/lipid-associating moiety coupled to polypeptide by residue.

DC A96 B04 D16
 IN HUSTON, J S; LAURENT, O; MARASCO, W A; SCHERMAN, D; WILS, P; ZHU, Q; QUAN, Z
 PA (HUST-I) HUSTON J S; (LAUR-I) LAURENT O; (MARA-I) MARASCO W A; (SCHE-I) SCHERMAN D; (WILS-I) WILS P; (ZHUQ-I) ZHU Q; (QUAN-I) QUAN Z
 CYC 96
 PI WO 2002000914 A2 20020103 (200231)* EN 96p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
 SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2001070142 A 20020108 (200235)
 US 2002132990 A1 20020919 (200264)
 ADT WO 2002000914 A2 WO 2001-US20182 20010625; AU 2001070142 A AU 2001-70142
 20010625; US 2002132990 A1 Provisional US 2000-213653P 20000623, US
 2001-888721 20010625
 FDT AU 2001070142 A Based on WO 2002000914
 PRAI US 2000-213653P 20000623; US 2001-888721 20010625
 AB WO 200200914 A UPAB: 20021031

NOVELTY - A gene-delivery compound (I) comprising a single-chain binding polypeptide (SCBP) having at least one effector segment having a cysteinyl residue and a nucleic acid-binding moiety (NABM) or a lipid-associating moiety (LAM) coupled to SCBP by the residue, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition (II) comprising (I) and a nucleic acid associated reversibly with NABM, or a liposome in association with LAM.

ACTIVITY - None given in the source material.

MECHANISM OF ACTION - Gene therapy. No supporting data is given.

USE - (I) is useful for targeted gene delivery for treating diseases by gene therapy.

ADVANTAGE - (I) is utilized to provide targeted non-viral delivery of gene to target cells, and (I) having the ability to bind to multiple, different surface markers on a target cell, can be utilized for multi-site targeting.

Dwg.0/26

TECH UPTX: 20020516
 TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Compound: In (I), the binding region of SCBP is effective in binding two or more surface markers of a mammalian cell, and comprises a single-chain Fv protein, where the marker is a tumor antigen from erbB-2, erbB-3, erbB-4, p53, p21 ras, transferrin receptor, Lewis Y antigen, carcinoembryonic antigen, epidermal growth factor, MUC1, and any other tumor-associated or tumor-specific antigen. NABM is preferably from salmon protamine, subfragments of salmon protamine, human histone H1, subfragments of human histone H1, human protamine, subfragments of human protamine, HMG, polylysine or any other DNA binding polypeptide; and LAM is from linear, branched, cyclic, and polycyclic compounds capable of insertion into and retention of lipid-containing compositions, where LAM contains polyethylene glycol (PEG) and preferably is maleimide-PEG-(C18)2, in which the PEG portion has about 10-100 oxyethyl units. (I) further comprises an additional effector segment that binds reversibly with nucleic acids, or that facilitates endosomal escape or avoidance, non-endosomal transport in a cell, or entry into the nucleus of a targeted cell, where the effector segment is a human histone H1 peptide sequence which comprises the carboxyl-terminal sequence that binds to the KDEL receptor in the Golgi, SEKDEL, or comprises SV40

large T antigen nuclear localization sequence, TPPKKKRKV. (I) further comprises a spacer sequence which is located between the effector segment containing the cysteinyl residue and an additional effector segment, where the spacer sequence comprises one or two segments of SSSSG or GGGGS. In (I), the cysteinyl residue is coupled to NABM by a heterobifunctional **crosslinking** agent which is preferably from succinimidyl trans-4(maleimidylmethyl)-cyclohexane-1-carboxylate (**SMCC**) and sulfo**SMCC**.

Preferred Composition: In (II), the nucleic acid comprises **DNA** encoding a therapeutic gene which is a lymphokine, a tumor necrosis factor, or an intrabody; or is from tumor suppressor genes, p53, proapoptotic genes, suicide genes, prodrug converting genes, HSV-TK and anti-angiogenic genes. In (II) comprising a liposome, SCBP is located on a surface of the liposome which is a stealth liposome.

L35 ANSWER 9 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2002-216898 [27] WPIDS

DNC C2002-066275

TI New integrase inhibiting compounds useful for development of anti-viral therapeutics comprises a **linker** group, a functional group bonded to **linker** group, and a bond between functional and **linker** groups.

DC B04 B05 D16

IN HARRISON, R W; SKALKA, A M

PA (UYJE-N) UNIV JEFFERSON THOMAS

CYC 21

PI WO 2002002516 A2 20020110 (200227)* EN 42p

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

W: CA JP

ADT WO 2002002516 A2 WO 2001-US19923 20010622

PRAI US 2000-215474P 20000630

AB WO 200202516 A UPAB: 20020429

NOVELTY - An integrase inhibiting compound (I) comprises a **linker** group (a), a functional group (b) bonded to (a) and a bond (c) between (b) and (a). (a) comprises a rigid aromatic or nonaromatic compound, (b) comprises at least one derivatized mono or polycyclic aromatic group (preferably aromatic phenyl naphthyl group) and (c) comprises a flexible **linkage**.

DETAILED DESCRIPTION - An integrase inhibiting compound (I) comprises a **linker** group (a), a functional group (b) bonded to (a) and a bond (c) between (b) and (a). (a) comprises a rigid aromatic or nonaromatic compound with at least one (b) replacing an atom of the rigid aromatic or non-aromatic compound. (b) comprises at least one derivatized mono or polycyclic aromatic group (preferably aromatic phenyl naphthyl group) and (c) comprises a flexible **linkage**.

An INDEPENDENT CLAIM is included for inhibiting an integrase involving binding (I) to an integrase, inhibiting a catalytic activity of the integrase and then inhibiting an essential function in viral replication of the retrovirus.

ACTIVITY - Anti HIV.

MECHANISM OF ACTION - HIV (human immuno deficiency virus) and ASLV (avian sarcoma-leukosis virus) integrase inhibitors. Hela cells (5 multiply 104) were plated and were analyzed for each concentration. On the following day, a HIV-based retroviral vector containing lacZ receptor gene described in Naldinin et al. Science, 272: 263 - 267, 1996 was added to each well for 2 hours in the presence of RWH35 (7-amino, 4-hydroxy, 2-naphthalene sulfonic acid and 1 equivalent of alpha, alpha'-dibromomethyl meta-xylene dissolved in DMSO (i.e. inhibitor compound)) and dextran (5 mg/ml). After 2 hours, the HIV vector was removed and fresh medium containing the inhibitor was added. Inhibitor was kept on cells for

another 16 hours, then removed and fresh medium added. Cells were stained 2 days post infection using a beta -gal assay performed according to the transfection **MBS** (mammalian transfection kit) (stratagene). The compound had an IC50 value of 0.7 micro M for HIV integrase.

USE - For inhibiting integrase and for further development of a therapeutic agent that causes inhibition of the integrase (claimed) essential in the life cycle of retroviruses.

ADVANTAGE - The compound inhibits the integrase, essential in the life cycle of retroviruses; allows the examination of the HIV integrase binding site and subsequently the mechanism of inhibition of enzyme activity. The compound has a restricted conformation for the determination of the integrase binding site and mechanism of inhibition and is effective in the submicromolar range and provides new lead compounds for the development of anti-viral therapeutics. The compound inhibits catalytic activity of the integrase thus inhibiting an essential function in viral replication of the retrovirus.

Dwg.0/7

TECH

UPTX: 20020429

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Functional Group: (b) further comprises mimicking nucleotides or bases of a **DNA** comprising placement into a stable hydrogen bonding and base stacking geometry on the integrase.

Preferred Method: (I) binds at or close to the active site on the integrase binds in a site distal or distinct from the **DNA** binding site on the integrase binds directly to a viral **DNA** -integrase complex or to a viral and host **DNA**-integrase complex.

(I) inhibits the integrase by inhibiting a viral integration, a viral **DNA** into a host **DNA**. The method further involves an inhibition of a processing step of the integration of the viral **DNA** into the host **DNA**. The inhibition of the integrase further involves inhibition of replication of a virus at concentrations below cell toxicity.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compound: (I) comprises a symmetric or an asymmetric compound. The compound comprises a mixture of 8-bromo, 7-amino, 4-hydroxy, 2-naphthalene sulfonic acid; diaminomethyl meta-xylene **linker** group with two functional groups comprising 7-amino, 4-hydroxy, 2-naphthalene sulfonic acid (preferably 8-bromo, 7-amino, 4-hydroxy, 2-naphthalene sulfonic acid).

Preferred Components: (b) is selected from para-aminobenzamidine; para-amino benzoic acid; 2,6-diaminoanthraquinone; 5-amino, 8-hydroxy quinoline; and 7-amino, 4-hydroxy, 2-naphthalene sulfonic acid. (a) is selected from meta-xylene, para-xylene, 2,6-dimethylpyridine or 1,4-diamino-2,3-butanediol. The rigid aromatic compound is a planar rigid aromatic compound.

L35 ANSWER 10 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2002-106127 [14] WPIDS

DNC C2002-032542

TI Novel vector comprising double stranded DNA having target sequence and chimeric molecule comprising sequence specific polyamide moiety bound non-covalently to target and ligand moiety covalently **linked** to polyamide.

DC B04 D16

IN BIANCHI, E; FATTORI, D; INGALLINELLA, P; KINZEL, O; PESSI, A

PA (RICE-N) IST RICERCHE BIOL MOLECOLARE ANGELETTI; (BIAN-I) BIANCHI E; (FATT-I) FATTORI D; (INGA-I) INGALLINELLA P; (KINZ-I) KINZEL O; (PESS-I) PESSI A

CYC 24

PI WO 2001088160 A2 20011122 (200214)* EN 98p

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

W: AU CA JP US

AU 2001058708 A 20011126 (200222)

EP 1290198 A2 20030312 (200320) EN

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR

US 2003207400 A1 20031106 (200374)

ADT WO 2001088160 A2 WO 2001-IB980 20010511; AU 2001058708 A AU 2001-58708 20010511; EP 1290198 A2 EP 2001-932034 20010511, WO 2001-IB980 20010511; US 2003207400 A1 WO 2001-IB980 20010511, US 2003-276734 20030512

FDT AU 2001058708 A Based on WO 2001088160; EP 1290198 A2 Based on WO 2001088160

PRAI GB 2000-11938 20000517

AB WO 200188160 A UPAB: 20020301

NOVELTY - A vector (conjugate) (I) comprising a double-stranded DNA (dsDNA) (Ia) having at least one target sequence (T); and a chimeric molecule (Ib) which comprises (i) a sequence specific polyamide (SSP) moiety bound non-covalently to (T); and (ii) a ligand moiety (L) covalently **linked** to SSP, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a composition comprising (I) and a carrier;
- (2) synthesis (M1) of SSP on a solid support involving:
 - (a) attaching an N-terminal of the polyamide to the solid support via a safety-catch **linker**, -S(=O)₂-NH-; and
 - (b) following synthesis of the polyamide, removing it from the solid support by cleavage of the safety-catch **linker** by activation and nucleophilic attachment;
- (3) introducing (M2) a dsDNA into a cell or a sub-cellular compartment involving:
 - (a) providing (Ib) which comprises SSP and (L) **linked** covalently to the SSP moiety, and capable of being directed to the cell or the sub-cellular compartment;
 - (b) providing a dsDNA which includes a target sequence for the SSP moiety, under conditions where (Ib) binds to the dsDNA to provide a vector; and
 - (c) bringing the vector into contact with the cell under conditions for uptake of the vector and transport of the dsDNA;
- (4) a eukaryotic cell obtained by (M2); and
- (5) progeny of a eukaryotic cell obtained by (M2).

ACTIVITY - Antibacterial; Virucide.

MECHANISM OF ACTION - Gene therapy; Vaccine.

No biological data given.

USE - (I) Is useful in a method of treatment of the human or animal body and for preparing a medicament for treating a condition treatable by gene therapy. (I) Is also useful in gene therapy techniques. (M2) is useful for introducing a dsDNA into the nucleus of a eukaryotic cell which involves providing (Ib) which comprises SSP and (L) **linked** covalently to SSP moiety and capable of being directed to the nucleus of the eukaryotic cell; providing a dsDNA which includes a target sequence for the SSP moiety, under conditions where (Ib) binds to the dsDNA provide a vector; and bringing the vector into contact with the eukaryotic cell under conditions for uptake of the vector and transport of the dsDNA. The vector is brought into contact with the eukaryotic cell in vivo, ex vivo or in vitro. The eukaryotic cell is preferably a CHO cell (all claimed). (I) is also used to deliver **DNA** encoding antigens (viral antigens, bacterial antigens or host **protein** antigens) useful as vaccines.

Dwg.0/4

TECH

UPTX: 20020301

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) Is synthesized by the process which includes the step of synthesis of SSP by (M1).

Preferred Vector: (I) Further comprises one or more sequences designed to facilitate homologous recombination to a specific locus within a host cell. (I) Comprises two or more (Ib) which comprise different ligand moieties. (Ia) has more than one (T) (in the range of 2-100, and preferably 6-10 target sequences), which is not present in the promoter or coding sequence part of the vector. (T) is at least 6 bases in length, preferably 10-20 bases in length. (Ia) Is linear, circular or a circular supercoiled DNA. (Ia) Further comprises dsDNA sequences of human, non-human animal, vegetable, bacterial or viral origin, and also comprises one or more transcribable sequences from promoters, and origins of replication, one or more selectable or detectable markers. (Ia) Comprises a transcribable DNA sequence which, when transcribed from the DNA under the control of a promoter (a) brings about an therapeutic effect, (b) yields mRNA for the expression of a **protein**, or (c) yields RNA which itself has a function as an anti-sense RNA or a ribozyme. (Ia) Comprises one or more coding sequences designed to modify tumor cells so that the tumor cells may be destroyed or inactivated. (Ia) Further comprises (a) one or more genes encoding enzymes capable of activating pro-drugs into active toxic drugs, (b) one or more tumor suppressor genes, (c) genes encoding cytokines or cell surface markers of immunoglobulin superfamily, (d) one or more functional copies of a gene, (e) DNA antigens useful as vaccines, or (f) one or more consecutive promoters and tissue specific promoters. SSP comprises at least 6 organic heterocyclic groups at least some of which are pyrrole and imidazole groups, preferably at least 7 organic heterocyclic groups (e.g. optionally substituted pyrrole, imidazole, pyrazole, triazole, furan, thiophene, oxazole, thiazole, or cyclopentadiene) or comprises 8-30 (preferably 18) organic cyclic groups. At least 60% (preferably 100%) of the organic cyclic groups or the organic heterocyclic groups which have 5 or 6 (preferably 5) annular members. The organic heterocyclic groups have 1-3 annular heteroatoms such as nitrogen, oxygen or **sulfur**. The organic heterocyclic **groups** have 1-2 annular nitrogen heteroatoms, and are preferably optionally substituted pyridine, pyrimidine, or triazine, where one or more annular NH groups are substituted with 1-3C alkyl groups (preferably Me). SSP comprises the organic heterocyclic groups (N-methyl pyrrole (Py) or N-methyl imidazole) having 5 annular members, and 1-2 annular nitrogen atoms of which one is methylated. The SSP further comprises one or more (2-6, preferably 4) optionally substituted aliphatic **amino acid groups** (e.g. glycine, beta alanine or gamma amino butyric acid) having a chain of 2-6 carbon atoms. The SSP comprises the optionally substituted **amino acid group** having a chain of 2-6 carbon atoms, proximal to one terminus of the moiety. (I) Comprises no consecutive sequence of 6 heterocycles, and where the organic cyclic **groups** and aliphatic **amino acid groups**, if present, are joined by **linking** groups having a length of 2 atoms where at least some of the **linking** groups will have NH groups. The **linking** groups are preferably methyleneamino (-CH₂-NH-), carboxamide (-C(=O)NH-), ethylene (-CH₂CH₂-), thiocarboxamide (-C(=S)NH-), or carboxamidinoyl (-C(=NH)NH-). Preferably, the **linking** groups are carboxamide (preferred), thiocarboxamide, or carboxamidinoyl. One or both of termini of SSP has a polar **group** (e.g. **amino**, hydroxyl, or mercapto) substituted on an alkyl group, where the polar group is from 2-6 carbon atoms from the **linkage** to the remaining molecule. At pH less than 8, the **amino group** is positively charged. Alternately, the polar group may also be optionally substituted aminopropyl or N-methylaminopropyl, where the SSP has one or two complementary pairs, each of which includes a N-methyl imidazole group and specificity of one nucleotide. (L) is capable of directing the **conjugate** to a

cellular or subcellular location, preferably to the nucleus of a eukaryotic cell, in which case the ligand moiety is a general nuclear localization signal. (L) (a) is a **protein** or **polypeptide** capable of binding a target receptor, (b) is a **protein** or **polypeptide** based on hormones or other signaling **proteins** which bind to a target on the surface of a cell, or (c) comprises a hybrid **protein** which includes a component to direct the **conjugate** to a particular target cell, and a component to promote uptake of the **conjugate** by the cell. (L) is insulin, asialoglycoprotein or its synthetic analogues, transferrin, malaria circumsporozoite **protein**, RGD analogues or endoosmotic **peptide**. The ligand moiety is a growth factor which binds to a receptor, or is an antibody or its fragment. (L) is a carbohydrate or mannose.

Preferred Method: In (M1), the safety catch **linker** comprises a **linkage** -C(=O)-CH₂CH₂CH₂-S(=O)₂-NH-, -C(=O)-CH₂CH₂CH₂-S(=O)₂-NH-C(=O)-. The activation is achieved by reaction with iodoacetonitrile. The nucleophilic attack is achieved by reaction with amine or thiol. The polyamide is synthesized using one or more of the reagents (R1), (R2) or (R3) as given in the specification.

L35 ANSWER 11 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 2001-308249 [32] WPIDS
 CR 1997-558673 [51]
 DNC C2001-095229
 TI New lipid vesicle having a bilayer membrane that has a positive net charge at physiological pH for use in cosmetic, pharmaceutical or diagnostic applications.
 DC B04 B07
 IN GLUECK, R; KLEIN, P; WALTI, E R; WAELTI, E R
 PA (NIKA-N) NIKA HEALTH PROD LTD
 CYC 94
 PI WO 2001026628 A1 20010419 (200132)* EN 44p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
 AU 2000077850 A 20010423 (200147)
 NO 2002001607 A 20020607 (200250)
 EP 1217990 A1 20020703 (200251) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 SK 2002000478 A3 20020910 (200274)
 CZ 2002001216 A3 20021016 (200279)
 HU 2002002809 A2 20021228 (200308)
 KR 2002063872 A 20020805 (200308)
 JP 2003512306 W 20030402 (200325) 43p
 EP 1217990 B1 20040128 (200410) EN
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
 ADT WO 2001026628 A1 WO 2000-EP9540 20000929; AU 2000077850 A AU 2000-77850
 20000929; NO 2002001607 A WO 2000-EP9540 20000929, NO 2002-1607 20020405;
 EP 1217990 A1 EP 2000-967824 20000929, WO 2000-EP9540 20000929; SK
 2002000478 A3 WO 2000-EP9540 20000929, SK 2002-478 20000929; CZ 2002001216
 A3 WO 2000-EP9540 20000929, CZ 2002-1216 20000929; HU 2002002809 A2 WO
 2000-EP9540 20000929, HU 2002-2809 20000929; KR 2002063872 A KR
 2002-704325 20020404; JP 2003512306 W WO 2000-EP9540 20000929, JP
 2001-529418 20000929; EP 1217990 B1 EP 2000-967824 20000929, WO
 2000-EP9540 20000929
 FDT AU 2000077850 A Based on WO 2001026628; EP 1217990 A1 Based on WO

2001026628; SK 2002000478 A3 Based on WO 2001026628; CZ 2002001216 A3
Based on WO 2001026628; HU 2002002809 A2 Based on WO 2001026628; JP
2003512306 W Based on WO 2001026628; EP 1217990 B1 Based on WO 2001026628
PRAI US 1999-414872 19991008
AB WO 200126628 A UPAB: 20040210

NOVELTY - A lipid vesicle having a bilayer membrane that has a positive net charge at physiological pH. The vesicle further comprises at least one active fusogenic peptide and optionally phosphatidylethanolamine (PE) and/or cationic lipids other than 1,3-dioleoyloxy-2-(6-carboxy-spermyl)-propylamide (DOSPER).

DETAILED DESCRIPTION - A lipid vesicle having a bilayer membrane that has a positive net charge at physiological pH, the vesicle further comprises at least one active fusogenic peptide that is a non-Sendai viral hemagglutinin that causes the vesicles to be internalized by target cells through receptor-mediated phagocytosis or endocytosis, characterized in that the vesicle membrane comprises 5-30% by weight, based on total membrane lipids of DOSPER and a balance of 95-70% by weight of other lipids comprising phosphatidylcholine (PC) or a derivative and optionally phosphatidylethanolamine (PE) and/or cationic lipids other than DOSPER.

INDEPENDENT CLAIMS are also included for:

(1) a process for the manufacture of a lipid vesicle, which comprises;

(1) preparing a buffer solution that comprises a non-ionic detergent and that further comprises DOSPER and other lipids and at least one active fusogenic peptide that is a non-Sendai viral hemagglutinin that causes the vesicles to be internalized by target cells through receptor-mediated phagocytosis or endocytosis;

(2) adjusting the lipid concentration to 5-30% by weight of DOSPER and to a balance of 95-70% by weight of other lipids comprising PC or a derivative and optionally PE and/or cationic lipids other than DOSPER; and

(3) removing the detergent by dialysis or by treating the solution with microcarrier beads, resulting in the formation of positively charged lipid bilayer vesicles; and

(2) use of a vesicle for the manufacture of a composition for cosmetic, diagnostic or medical applications, particularly for delivering a desired drug or substance to resting or proliferating target cells.

USE - A composition comprising more than one vesicle can be used in cosmetic, pharmaceutical or diagnostic applications (claimed). The target cells are selected from the group consisting of cancer cells, leukemic cells and virally infected cells.

ADVANTAGE - When using DOSPER as a cationic lipid in combination with other lipids, high performance virosomes can be produced that even exceed up to ten times the already high transfection efficiency of the N-((1,2,3-dioleoyloxy)-propyl)-N,N,N-trimethylammoniummethyl-sulfate (DOTAP) virosomes of WO97/41834.

Dwg.0/13

TECH

UPTX: 20010611

TECHNOLOGY FOCUS - BIOLOGY - Preferred components: The vesicle further contains a desired drug or substance (I) for delivery to target cells, which is preferably negatively charged and particularly selected from a group consisting of a dye, a tracer substance, a cosmetic agent, and a nucleic acid material, selected from a group consisting of short chain DNA or RNA, deoxyribonucleotides, oligodeoxyribonucleotides, oligodeoxyribonucleotide selenoates, oligodeoxyribonucleotide phosphorothioates, oligodeoxyribonucleotide phosphoramidates, oligodeoxyribonucleotide methylphosphonates, **peptide** nucleic acids, ribonucleothioates, oligoribonucleotides, oligoribonucleotide phosphorothioates, 2'-Ome-oligoribonucleotide phosphates, 2'-Ome-oligoribonucleotide phosphorothioates, ribozymes, genes, plasmids and vectors.

The nucleic acid material preferably comprises at least one antisense **oligonucleotide**, preferably an antisense **oligonucleotide** that is targeting protooncogene or oncogene encoded mRNA. The vesicle further comprises at least one cell-specific marker attached to the vesicle membrane, which further comprises PE and a bifunctional **crosslinker** which is **linked** with one of its binding sites to a free **amino group** of the PE and with its other binding site to the cell specific marker. The cell-specific marker is a **protein** for binding to a receptor of target cells selected from the group consisting of an antibody, an antibody fragment, a cytokine and a growth factor.

The hemagglutinin is derived from a virus selected from the group consisting of rhabdovirus, parainfluenza virus type III, Semliki Forest virus and togavirus.

The non-ionic detergent is octaethyleneglycol monododecylether (C12E8) or n-octyl-oligoxyethylene.

The **crosslinking** agent is a heterobifunctional organic molecule having at least one maleimido and at least one carboxyl group, and is preferably selected from the group consisting of bis-N-succinimidyl derivatives and photactivatable succinimidyl derivatives.

Preferred compositions: The vesicle comprises the nucleic acid material in an amount 0.03-0.1, preferably 0.045-0.065 microg per 1 microg DOSPER. The average vesicle diameter is 120-180 nm. The vesicle membrane comprises DOSPER in a concentration of 10-30%, preferably 20-25% by weight, based on total membrane lipids. The vesicle membrane comprises 25% by weight of DOSPER and 75% by weight of PC, preferably dioleoylphosphatidylcholine (DOPC).

Preparation: The process for the manufacture of the lipid vesicle further comprises:

(a) incorporating a quantity of (I) for delivery to target cells into the vesicles; and

(b) preparing **conjugate** molecule complexes consisting of phosphatidylethanolamine (PE), a bifunctional **crosslinker**, and a cell-specific marker in a way such that the bifunctional **crosslinker** with one binding site **links** to the **amino group** of PE and with another one to a **thiol group** of the cell-specific marker, removing unconjugated material and adding molecule complexes to the solution of step (1).

Incorporation of (I) is accomplished by adding it to the solution in step (1) and in step (3) vesicles containing (I) are formed. Incorporation of (I) into the vesicles is preferably accomplished by adding to the vesicles from (3), sonicating the mixture to integrate (I) into the vesicles and removing non-integrated material, preferably by gel filtration.

Positively charged lipid complexes or liposomes, comprising 50-100% by weight, based on their total lipid contents, of DOSPER lipid, with (I) can be added to the vesicles.

The manufacture of the composition, comprises incubating target cells in vitro in the presence of the vesicle and optionally transferring the incubated target cells to an organism in vivo. Metabolic or proliferative activity of the target cells is reduced upon incubation in the presence of the vesicle.

L35 ANSWER 12 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 2001-273770 [28] WPIDS
 DNN N2001-195557 DNC C2001-083075
 TI New modified peptide nucleic acids and **oligonucleotides**, useful for treating and preventing bacterial infections and disinfecting non-living objects.
 DC B04 D16 D22 P34

IN BECK, F; GIWERCMAN, B K; GOOD, L; HANSEN, H F; MALIK, L; NIELSEN, P E;
SCHOU, C; WISSENBAACH, M

PA (PANT-N) PANTHECO AS; (NIEL-I) NIELSEN P E; (BECK-I) BECK F; (GIWE-I)
GIWERCMAN B K; (GOOD-I) GOOD L; (HANS-I) HANSEN H F; (MALI-I) MALIK L;
(SCHO-I) SCHOU C; (WISS-I) WISSENBAACH M

CYC 95

PI WO 2001027261 A2 20010419 (200128)* EN 73p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000077730 A 20010423 (200147)
NO 2002001711 A 20020611 (200252)
EP 1220902 A2 20020710 (200253) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI

BR 2000014756 A 20020709 (200254)
HU 2002003465 A2 20030128 (200323)
CN 1387567 A 20021225 (200324)
US 6548651 B1 20030415 (200329)
JP 2003511466 W 20030325 (200330) 99p
US 2003176325 A1 20030918 (200362)
ZA 2002002455 A 20030827 (200362) 109p
US 2003199431 A1 20031023 (200370)

ADT WO 2001027261 A2 WO 2000-DK580 20001013; AU 2000077730 A AU 2000-77730
20001013; NO 2002001711 A WO 2000-DK580 20001013, NO 2002-1711 20020411;
EP 1220902 A2 EP 2000-967618 20001013, WO 2000-DK580 20001013; BR
2000014756 A BR 2000-14756 20001013, WO 2000-DK580 20001013; HU 2002003465
A2 WO 2000-DK580 20001013, HU 2002-3465 20001013; CN 1387567 A CN
2000-815281 20001013; US 6548651 B1 Provisional US 1999-159679P 19991015,
Provisional US 1999-159684P 19991015, Provisional US 2000-211435P
20000614, Provisional US 2000-211758P 20000614, Provisional US
2000-211878P 20000614, US 2000-689155 20001012; JP 2003511466 W WO
2000-DK580 20001013, JP 2001-530466 20001013; US 2003176325 A1 Provisional
US 1999-159679P 19991015, Provisional US 1999-159684P 19991015,
Provisional US 2000-211435P 20000614, Provisional US 2000-211758P
20000614, Provisional US 2000-211878P 20000614, Div ex US 2000-689155
20001012, US 2001-83259 20011019; ZA 2002002455 A ZA 2002-2455 20020327;
US 2003199431 A1 Provisional US 1999-159679P 19991015, Provisional US
1999-159684P 19991015, Provisional US 2000-211435P 20000614, Provisional
US 2000-211758P 20000614, Provisional US 2000-211878P 20000614, Div ex US
2000-689155 20001012, US 2002-109274 20020327

FDT AU 2000077730 A Based on WO 2001027261; EP 1220902 A2 Based on WO
2001027261; BR 2000014756 A Based on WO 2001027261; HU 2002003465 A2 Based
on WO 2001027261; JP 2003511466 W Based on WO 2001027261; US 2003199431 A1
Div ex US 6548651

PRAI US 2000-211878P 20000614; DK 1999-1467 19991013; DK 1999-1471
19991013; US 1999-159679P 19991015; US 1999-159684P 19991015; DK
1999-1734 19991203; DK 1999-1735 19991203; DK 2000-522
20000328; DK 2000-670 20000419; DK 2000-671 20000419; US
2000-211435P 20000614; US 2000-211758P 20000614

AB WO 200127261 A UPAB: 20010522
NOVELTY - A modified peptide nucleic acid (PNA), is new.
DETAILED DESCRIPTION - A modified peptide nucleic acid (PNA) (I) of
formula (F1), is new.
Peptide-L-PNA (F1), where
L = **linker** or a bond;
Peptide = any amino acid sequence; and

PNA = Peptide nucleic acid and a pharmaceutically acceptable salt.
INDEPENDENT CLAIMS are also included for the following:

- (1) a modified peptide nucleic acid (PNA) of formula (F1);
- (2) a modified **oligonucleotide** (II) of formula Peptide-L-Oligon (F2);
- (3) a modified PNA molecule (III) comprising one of 120 fully defined sequences as given in the specification such as H-KFFKFFKFFK-ado-CAT AGC TGT TTC-NH₂, H-FFKFFKFFK-ado-CAT AGC TGT TTC-NH₂ and H-FKFFKFFK-ado-CAT AGC TGT TTC-NH₂;
- (4) use of (I)-(III) (in the manufacture of a medicament) for the treatment of infectious diseases, such as bacterial infections;
- (5) treating an infectious disease comprising administering to a patient (I), (II) or (III);
- (6) disinfecting (M1) non-living objects comprising administering one or more (I), (II) or (III);
- (7) use of (I) or (III) in the identification of PNA sequences which are effective in blocking essential functions in bacteria, where different PNA sequences are incorporated in the modified PNA molecule and tested for their ability to inhibit or reduce bacterial growth; and
- (8) identifying a PNA sequence, which is useful in inhibiting or reducing bacterial growth comprising mixing (I) or (III) containing different PNA sequences with bacteria, where the selected PNA sequences are complementary to nucleotide sequences for the bacteria and identifying the PNA sequences which are effective in inhibiting or reducing bacterial growth.

ACTIVITY - Antibacterial.

(I) and (III) were tested for antibacterial effect in vivo according to the test described by N. Frimodt-Moller. Untreated animals developed fulminant clinical signs of infection. At all time points (I) and (III) suppressed the Escherichia coli cell forming units/ml compared to non-treated controls and was as efficient as the 2 positive controls.

MECHANISM OF ACTION - Antisense therapy.

USE - (I)-(III) are useful for disinfecting non-living objects and for treating or preventing infectious diseases (claimed), particularly those caused by microorganisms resistant to antibiotics, such as methicillin-resistant and methicillin-vancomycin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus faecalis and Enterococcus faecium, penicillin-resistant Streptococcus pneumoniae and cephalosporin and quinolone resistant gram negative rods e.g. Escherichia coli, Klebsiella pneumoniae, Pseudomonas and Enterobacter species.

ADVANTAGE - PNA polyamide backbones are not recognized by nucleases or proteases and as a result are resistant to degradation by enzymes unlike nucleic acids and peptides.

Dwg.0/7

TECH

UPTX: 20010522

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Compound: The **linking** group in (III) is -achc-beta.ala-, -achc-ado-, -lcsbcc-beta.ala-, -mbs-beta.ala-, -emcs-beta.ala-, -lcsbcc-ado-, -mbs-ado-, -emcs-ado- or -smph-ado-. Preferably the peptide is (KFF)3K and subunits comprising at least 3 amino acids, particularly (KFF)3.

Preferred Method: M1 is useful for disinfecting surgery tools, hospital inventory, dental tools, slaughterhouse inventory and tools or dairy inventory and tools.

L35 ANSWER 13 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-138654 [14] WPIDS
CR 2002-188688 [24]
DNC C2001-041027
TI New isolated polynucleotide useful for outer membrane vesicle preparation

from Gram-negative bacterial strain for vaccination of microbial infections.

DC B04 D16
IN BERTHET, F J; DALEMANS, W L J; DENOEL, P; DEQUESNE, G; FERON, C; LOBET, Y; POOLMAN, J; THIRY, G; THONNARD, J; VOET, P; DALEMANS, W L; LHONNARD, J; DENCEL, P
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (SMIK) SMITHKLINE BEECHAM BIOLOGICALS SA

CYC 95

PI WO 2001009350 A2 20010208 (200114)* EN 127p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000068336 A 20010219 (200129)
NO 2002000506 A 20020402 (200235)
BR 2000012974 A 20020507 (200238)
CZ 2002000403 A3 20020515 (200241)
EP 1208214 A2 20020529 (200243) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

KR 2002027514 A 20020413 (200267)
HU 2002003056 A2 20021228 (200308)
CN 1377415 A 20021030 (200314)
JP 2003506049 W 20030218 (200315) 189p
MX 2002001205 A1 20030701 (200366)
ZA 2002000824 A 20031126 (200402) 130p

ADT WO 2001009350 A2 WO 2000-EP7424 20000731; AU 2000068336 A AU 2000-68336 20000731; NO 2002000506 A WO 2000-EP7424 20000731, NO 2002-506 20020131; BR 2000012974 A BR 2000-12974 20000731, WO 2000-EP7424 20000731; CZ 2002000403 A3 WO 2000-EP7424 20000731, CZ 2002-403 20000731; EP 1208214 A2 EP 2000-956369 20000731, WO 2000-EP7424 20000731; KR 2002027514 A KR 2002-701441 20020201; HU 2002003056 A2 WO 2000-EP7424 20000731, HU 2002-3056 20000731; CN 1377415 A CN 2000-813842 20000731; JP 2003506049 W WO 2000-EP7424 20000731, JP 2001-514142 20000731; MX 2002001205 A1 WO 2000-EP7424 20000731, MX 2002-1205 20020201; ZA 2002000824 A ZA 2002-824 20020130

FDT AU 2000068336 A Based on WO 2001009350; BR 2000012974 A Based on WO 2001009350; CZ 2002000403 A3 Based on WO 2001009350; EP 1208214 A2 Based on WO 2001009350; HU 2002003056 A2 Based on WO 2001009350; JP 2003506049 W Based on WO 2001009350; MX 2002001205 A1 Based on WO 2001009350

PRAI GB 1999-18319 19990803
AB WO 200109350 A UPAB: 20040107

NOVELTY - An isolated polynucleotide sequence which hybridizes under highly stringent conditions to at least a 30 nucleotide portion of 80 sequences described in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

- (1) a genetically-engineered outer membrane vesicle (bleb) preparation from a Gram-negative bacterial strain characterized in that the preparation is obtainable by employing a process comprising:
 - (a) introducing a heterologous gene, optionally controlled by a strong promoter sequence, into the chromosome by homologous recombination; and
 - (b) making blebs from the strain;
- (2) a vaccine comprising a bleb preparation and a pharmaceutically acceptable excipient;
- (3) a vector suitable for performing recombination events;
- (4) a modified Gram-negative bacterial strain from which the bleb

preparation is made;

(5) an immuno-protective and non-toxic Gram-negative bleb, ghost, or killed whole cell vaccine suitable for paediatric use.

ACTIVITY - Antiviral; Antibacterial; Antifungal.

Animals were immunized three times with 5 micro g of the different OMVs absorbed on Al(OH)₃ on days 0, 14, and 28. Bleedings were done on days 28 and 35, and they were challenged on day 35. The challenge dose was 20 X LD₅₀ (approx. 10 to the power of 7 CFU/mouse). Mortality rate was monitored for 7 days after challenge.

OMVs injected were:

Group1: Cps-, PorA+

Group2: Cps-, PorA-

Group3: Cps-, PorA-, NspA+

Group4: Cps-, PorA-, Omp85+

Group5: Cps-, PorA-, Hsf+

24 hours after the challenge, there was 100% mortality in the negative control group, while mice immunized with the 5 different OMVs preparations were still alive. Sickness was also monitored during the 7 days and the mice immunized with the NSPA over-expressed blebs appeared to be less sick than the other groups. PorA present in PorA+ blebs is likely to confer extensive protection against infection by the homologous strain. However, protection induced by PorA-up-regulated blebs is likely to be due at least to some extent, to the presence of increased amount of NspA, OMP85 or Hsf.

MECHANISM OF ACTION - Vaccine.

USE - The claimed polynucleotide sequence is used in performing a homologous recombination event within 1000 base pairs upstream of a Gram-negative bacterial chromosomal gene in order to either increase or decrease expression of the gene. The bleb preparation is useful in the manufacture of a medicament for immunizing a human host against a disease caused by infection of one or more of the following: *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenza*, *Moraxella catarrhalis*, *Pseudomonas aeruginosa*, *Chlamydia trachomatis*, and *Chlamydia pneumonia*. The invention is useful for immunizing a human host against the diseases caused by the above. The invention also provides immunization against the influenza virus. Immuno-protective and non-toxic Gram-negative bleb, ghost, or killed whole cell vaccines are useful for paediatric use (all claimed).

ADVANTAGE - The vaccine is more immunogenic, less toxic, and safer.
Dwg.0/17

TECH

UPTX: 20010312

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: A genetically-engineered outer membrane vesicle (bleb) preparation from a Gram-negative bacterial strain characterized in that the preparation is obtainable by employing one or more processes selected from:

(a) reducing immunodominant variable or non-protective antigens within the bleb preparation comprising the steps of determining the identity of such antigen, engineering a bacterial strain to produce less or non of the antigen, and making blebs from the strain;

(b) upregulating expression of protective outer membrane **proteins** (OMP) antigens within the bleb preparation comprising the steps of identifying such antigen, engineering a bacterial strain so as to introduce a stronger promoter sequence upstream of a gene encoding the antigen such that the gene is expressed at a level higher than in the non-modified bleb, and making blebs from the strain;

(c) upregulating expression of conditionally-expressed, protective OMP antigens within the bleb preparation comprising the steps identifying such an antigen, engineering a bacterial strain so as to remove the repressive control mechanisms of its expression, and making blebs from the strain;

(d) modifying lipid A portion of bacterial LPS within the bleb

preparation, comprises identifying a gene involved in rendering the lipid A portion of LPS toxic, engineering a bacterial strain so as to reduce or switch off expression of the gene, and making blebs from the strain;

(e) modifying lipid A portion of bacterial LPS within the bleb preparation, comprises identifying a gene involved in rendering the lipid A portion of LPS less toxic, engineering a bacterial strain so as to introduce a stronger promoter sequence upstream of the gene such that the gene is expressed at a level higher than in the non-modified bleb, and making blebs from the strain;

(f) reducing lipid A toxicity within the bleb preparation and increasing the levels of protective antigens, comprises engineering the chromosome of a bacterial strain to incorporate a gene encoding a Polymixin A peptide, or a derivative or analogue of it, fused to a protective antigen, and making blebs from the strain; or

(g) creating conserved OMP antigens on the bleb preparation comprises the steps of identifying such antigen, engineering a bacterial strain so as to delete variable regions of a gene encoding the antigen, and making blebs from the strain; where one or more of the following processes may further be employed:

(h) reducing expression within the bleb preparation of an antigen which shares a structural similarity with a human structure and may be capable of inducing an auto-immune response in humans, comprises identifying a gene involved in the biosynthesis of the antigen engineering a bacterial strain so as to reduce or switch off expression of the gene; and making blebs from the strain; or

(i) upregulating expression of protective OMP antigens within the bleb preparation comprises the steps of identifying such antigen, engineering a bacterial strain so as to introduce into the chromosome one or more further copies of a gene encoding the antigen controlled by a heterologous, stronger promoter sequence, and making blebs from the strain.

The engineering steps of (a)-(e) and (h)-(i) are carried out by homologous recombination events between a sequence of at least 30 nucleotides on the bacterial chromosome, and a sequence of at least 30 nucleotides on a vector transformed within the strain. The engineering steps are carried out by double cross-over homologous recombination events between two sequences of at least 30 nucleotides on the bacterial chromosome separated by nucleotide sequence 'X', and two sequences of at least 30 nucleotides on a vector transformed within the strain separated by nucleotide sequence 'Y', where during the recombination event X and Y are interchanged. The two nucleotide sequences are of approximately the same length and the vector is linear DNA molecule. (a)-(e) and (h) are carried out within the region of the chromosome 1000 base pairs upstream of the initiation codon of the gene of interest. In (a), (d), and (h) nucleotide sequence X comprises part of the promoter region of the gene, and nucleotide sequence Y comprises either a weak promoter region, or no promoter region. In (b) or (e) nucleotide sequence Y comprises a strong promoter region for the bacterium. Y is inserted 200-600 base pairs, preferably 400 base pairs, upstream of the initiation codon of the gene of interest. In (c) nucleotide sequence X comprises part of the repressive control sequence of the promoter, and Y comprises no such sequence. The recombination events in (a), (d), and (h) are carried out such that nucleotide sequence X comprises part of the coding sequence of the gene of interest. The recombination events of (i) is carried out such that Y comprises the further copy of the gene within an expression cassette. The bleb preparation is preferably isolated from a modified *Neisseria meningitidis* B strain. Bleb is obtainable by employing at least (b) and/or (i) where one or more of the following genes are upregulated: NspA, Hsf-like, Hap, PorA, PorB, ONP85, PilQ, PldA, FrpB, TbpA, TbpB, FrpA, frpC, LpbA, LpbB, GhaB, HasT, lipo02, Tbp2 (lipo28), MltA (lipo30), and

ctrA.

In (a) one or more of the following genes are downregulated from: PorA, PorB, PilC, TbpA, TbpB, LbpA, LbpB, Opa, and Opc.

In (d) one or more of the following genes are downregulated from: htrB, msbB and lpxK.

In (e) one or more of the following are upregulated: pmrA, pmrB, pmrE, and pmrF.

In (c) the repressive control sequence of the promoter is the fur operator region of either or both the TbpB or LbpB genes.

In (h) one or more of the following genes are down regulated: galE, siaA, **siaB**, siaC, siaD, ctrA, ctrB, ctrC, and ctrD.

The bleb preparation may also be isolated from a modified Moraxella catarrhalis strain.

In this case in (b) and/or (i) one or more of the following genes are upregulated: OMP106, HasR, PilQ, OMP85, lipo06, lipo10, lipo11, P6, ompCD, CopB, D15, Omp1A1, Hly3, LbpA, LpbB, TbpA, TbpB, OmpE, UspA1, UspA2, and Omp21.

In (a) one or more of the following genes are down regulated: CopB, OMP106, OmpB1, TbpA, TbpB, LbpA, and LbpB.

In (d) one or more of the following genes are downregulated: htrB, msbB, and lpxK.

In (e) one or more of the following genes are upregulated: pmrA, pmrB, pmrE, and pmrF.

The bleb preparation may also be isolated from Haemophilus influenzae.

In this case in (b) and/ or (i) one or more of the following genes are upregulated: D15, P6, TbpA, TbpB, P2, P5, OMP26, HMW1-4, Hia, Hsf, Hap, Hin47, and Hif.

In (a) one or more of the following genes are downregulated: P2, P5, Hif, IgA1-protease, HgpA, HgpB, HMW1, HMW2, Hxu, TbpA, and TbpB.

In (d) one or more of the following genes are downregulated: htrB, msbB, lpxK.

In (e) one or more of the following genes are upregulated: pmrA, pmrB, pmrE, and pmrF.

The Gram-negative strain may be Neisseria gonorrhoeae, Haemophilus influenzae, or Moraxella catarrhalis and the heterologous gene is a protective OMP from Chlamydia trachomatis, Moraxella catarrhalis, and Haemophilus influenzae respectively.

Preferred Vaccine: The vaccine may be a meningococcal vaccine comprising the bleb preparation and one or more plain or **conjugated** meningococcal capsular polysaccharides selected from the serotypes A, C, Y or W. The vaccine may be a meningitis vaccine comprising the preparation, a **conjugated** H. influenzae b capsular polysaccharide, and one or more plain or **conjugated** pneumococcal capsular polysaccharides.

The vaccine may be a otitis media vaccine comprising the bleb preparation and one or more plain or **conjugated** pneumococcal capsular polysaccharides, and one or more antigens that can protect a host against non-typeable H. influenzae infection. The latter additionally comprises one or more **protein** antigens that can protect a host against Streptococcus pneumoniae and/or one or more antigens that can protect a host against RSV and/or one or more antigens that can protect a host against influenza virus.

Preferred Nucleotide: The nucleotide comprises at least 30 nucleotides, preferably at least 30 nucleotides from one of 80 sequences described in the specification of complements of them.

L35 ANSWER 14 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-071273 [08] WPIDS
DNN N2001-053932 DNC C2001-019975
TI Siah-Mediated Degradation Protein, useful for drug screening, for therapeutic applications and for functional genomics.

DC B04 D16 P14 S03
 IN MATSUZAWA, S; REED, J C
 PA (BURN-N) BURNHAM INST
 CYC 94
 PI WO 2000077207 A2 20001221 (200108)* EN 121p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
 LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG
 SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2000057303 A 20010102 (200121)
 EP 1185652 A2 20020313 (200225) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 JP 2003502042 W 20030121 (200308) 127p
 US 6638734 B1 20031028 (200372)#
 ADT WO 2000077207 A2 WO 2000-US15873 20000609; AU 2000057303 A AU 2000-57303
 20000609; EP 1185652 A2 EP 2000-942718 20000609; WO 2000-US15873 20000609;
 JP 2003502042 W WO 2000-US15873 20000609; JP 2001-503651 20000609; US
 6638734 B1 Provisional US 1999-367334P 19990611, US 2000-591694 20000609
 FDT AU 2000057303 A Based on WO 2000077207; EP 1185652 A2 Based on WO
 2000077207; JP 2003502042 W Based on WO 2000077207
 PRAI US 1999-330517 19990611; US 2000-591694 20000609
 AB WO 200077207 A UPAB: 20010207
 NOVELTY - Isolated nucleic acid (I) encoding a Siah-Mediated Degradation
 Protein (SMDP) and/or Skp1 Cullin F-box (SCF)-complex protein (SCP), or
 their functional fragment, is new.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
 following:
 (1) a vector (II) and a recombinant cell (III), containing (I);
 (2) an **oligonucleotide** (Ia) comprising at least 15
 nucleotides capable of specifically hybridizing to a nucleotide sequence
 (S1) comprising 1274, 1432, 1413, 1673, 1892, 1075 or 2037 nucleotides
 fully defined in the specification;
 (3) an antisense-nucleic acid (Ib) capable of specifically binding to
 mRNA encoded by (I);
 (4) a kit for detecting the presence of SMDP and/or SCP cDNA
 sequence, comprising (Ia);
 (5) an isolated SMDP and/or SCP characterized by its ability to bind
 at least one SMDP and/or SCP;
 (6) expressing SMDP and/or SCP;
 (7) an isolated anti-SMDP and/or SCP antibody (Ab) having specific
 reactivity with SMDP and/or SCP;
 (8) a composition comprising (Ib) effective to inhibit expression of
 human SMDP and/or SCP and an acceptable hydrophobic carrier capable of
 passing through a cell membrane;
 (9) a transgenic non-human mammal expressing (I);
 (10) identifying (I) by contacting a sample containing nucleic acid
 with (Ia) under high stringency hybridization conditions, and identifying
 the compounds that hybridize;
 (11) detecting the presence of human SMDP and/or SCP in a sample by
 contacting a test sample with Ab and detecting the presence of Ab-SMDP
 and/or SCP complex to detect the presence of SMDP and/or SCP in the
 sample;
 (12) single strand **DNA** primers for amplification of (I),
 comprising a nucleic acid sequence derived from S1;
 (13) a bioassay for evaluating whether test compounds are capable of
 acting as agonists or antagonists for SMDP and/or SCP protein or their
 functional fragments, involving culturing of cells containing (I) in the

presence of a test compound whose ability to modulate activity of SMDP and/or SCP such as protein:protein binding activity or protein degradation activity, is sought to be determined, and monitoring the cells for either an increase or decrease in the level of protein activity;

(14) a therapeutic composition (TC) comprising SMDP and/or SCP, their functional fragments, a compound identified the above said method, or Ab;

(15) inducing the degradation function of a target protein, by expressing a chimeric protein (CP) comprising a target-protein binding domain operatively **linked** to a protein degradation binding domain of a protein unit of the ubiquitin-mediated protein degradation family, in a cell;

(16) determining the function of a target protein, by expressing CP in a first cell, and comparing its phenotype to the phenotype of a control second cell;

(17) identifying a nucleic acid molecule encoding a protein that modulates a cellular phenotype, by expressing a chimeric nucleic acid comprising a unit of nucleic acid library fused to nucleic acid encoding a protein degradation binding domain of a protein unit of the ubiquitin-mediated protein degradation family, in a cell, and screening the cell for the modulation of the phenotype;

(18) a chimeric nucleic acid screened by the above said method;

(19) a nucleic acid library comprising a number of chimeric nucleic acids such that each chimeric nucleic acid comprises an SMDP and/or SCP or its functional fragment;

(20) treating a disease by degrading the function of a target protein, by introducing CP into a cell; and

(21) a chimeric protein comprising SMDP and/or SCP.

ACTIVITY - Cytostatic; antiinflammatory; antiarthritic; immunosuppressive; antibacterial.

No supporting data given.

MECHANISM OF ACTION - Modulator of SMDP and/or SCP activity.

No supporting data given.

USE - SMDP and/or SCP are useful for modulating the activity of oncogenic proteins. Agonists or antagonists of SMDP and/or SCP protein are useful for modulating the activity of SMDP and/or SCP protein as well as modulating protein degradation mediated by SMDP and/or SCP protein. TC is useful for treating a pathology characterized by abnormal cell proliferation and inflammation. (I) is useful as a probe for assaying the presence and/or the amount of SMDP and/or SCP gene or mRNA transcript in a given sample. (I) and (Ia) are also useful as primers and/or templates in PCR (polymerase chain reaction) for amplifying (I). SMDP and/or SCP proteins are useful in bioassays, and as immunogens for producing Ab. Bioassays are useful for monitoring SMDP and/or SCP levels and for diagnosing physiological disorders that result from abnormal levels of SMDP and/or SCP. SMDP and/or SCP are useful for treating cancer pathologies, keratin hyperplasia, keloid, neoplasia, benign prosthetic hypertrophy, inflammatory hyperplasia, bone marrow aplasia, immunodeficiencies and inflammatory diseases such as sepsis, fibrosis, arthritis and graft versus host diseases.

Dwg.0/10

TECH

UPTX: 20010207

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Sequence: (I) comprises a **DNA** encoding an amino acid sequence comprising 298, 228, 80, 443, 522, 327 or 447 amino acids fully defined in the specification, a **DNA** that hybridizes to the above **DNA** under moderately stringent conditions and encoding biologically active SMDP and/or SCP, or a **DNA** degenerate with respect to either of the above sequences and encoding a biologically active SMDP and/or SCP. (I) comprises a sequence that hybridizes under high stringent conditions to the SMDP and/or SCP coding portion of S1. (Ia) is labeled with detectable marker.

Ab is a monoclonal or polyclonal antibody. (I) is Sia-1alpha, SIP-L, SIP-S, SAF-1, SAF-2, and SAD, or their functional fragments. Preferred Method: (I) has been mutated and SMDP and/or SCP so expressed is not native to SMDP and/or SCP. Activity of SMDP and/or SCP is modulated by binding of Siah-1 to APC. The transgenic non-human animal expressing (I) is a mouse. (I) which modulates the phenotype such as cell proliferation, cell survival, cell death, cell secretion or cell migration, is screened.

L35 ANSWER 15 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 2000-549134 [50] WPIDS
 DNC C2000-163952
 TI Novel polypeptides containing pIgR-binding domains used for targeting and transport to the mucosal epithelia, in the treatment of disorders accessible to the mucosal epithelia, e.g. asthma.
 DC B04 D16
 IN CAPRA, J D; HEXHAM, J M; MANDECKI, W; WHITE, K
 PA (DGIB-N) DGI BIOTECHNOLOGIES; (OKLA-N) OKLAHOMA MEDICAL RES FOUND; (TEXA) UNIV TEXAS SYSTEM; (DGIB-N) DGI BIOTECHNOLOGIES INC
 CYC 91
 PI WO 2000047611 A2 20000817 (200050)* EN 137p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ TZ UG ZW
 W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
 FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
 LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
 TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2000027597 A 20000829 (200062)
 EP 1151000 A2 20011107 (200168) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 JP 2002539771 W 20021126 (200307) 166p
 AU 769259 B 20040122 (200412)
 ADT WO 2000047611 A2 WO 2000-US3650 20000211; AU 2000027597 A AU 2000-27597 20000211; EP 1151000 A2 EP 2000-906030 20000211, WO 2000-US3650 20000211; JP 2002539771 W JP 2000-598527 20000211, WO 2000-US3650 20000211; AU 769259 B AU 2000-27597 20000211
 FDT AU 2000027597 A Based on WO 2000047611; EP 1151000 A2 Based on WO 2000047611; JP 2002539771 W Based on WO 2000047611; AU 769259 B Previous Publ. AU 2000027597, Based on WO 2000047611
 PRAI US 1999-119932P 19990212
 AB WO 200047611 A UPAB: 20001010
 NOVELTY - A 10-50 residue peptide (I) comprising a pIgR-binding domain, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a fusion protein comprising a pIgR-binding domain covalently **linked** to a non-antibody peptide or polypeptide;
- (2) a polynucleotide encoding the fusion protein of (1);
- (3) targeting an agent to a mucosal epithelium comprising administering to a mammal a targeting complex comprising the agent and (I), the complex binds to, and is taken up by, cells expressing pIgR, and is transported to the mucosal epithelium;
- (4) targeting a non-antibody peptide or polypeptide to a mucosal epithelium, comprising administering the fusion protein of (1) to a mammal, the protein binds to, and is taken up by, cell expressing pIgR, and is transported to the mucosal epithelium;
- (5) delivering an agent to a cell, comprising contacting (I) with a cell expressing pIgR; and
- (6) delivering a non-antibody peptide or polypeptide to a cell, comprising contacting the fusion protein of (1) with a cell expressing

pIgR.

ACTIVITY - Antiasthmatic; antiinflammatory; antiinfectious; cytostatic; antiulcer; antidiarrheal; hepatropic; virucide; vasotropic; anti-human immunodeficiency virus; antibacterial. No biological data is given.

MECHANISM OF ACTION - None given.

USE - For targeting and transport to the mucosal epithelium (claimed), for the prevention or treatment of diseases, ailments or conditions that are accessible to mucosal epithelia, including asthma, bronchitis, emphysema, cystic fibrosis, bronchiectasis, bronchiolitis, pulmonary edema, viral tracheobronchitis, sleep apnea syndrome, infectious diseases, neoplastic conditions, Loffler's syndrome, kyphocliosis, dysphagia, peptic ulcers, diarrheal diseases, ulcerative colitis, Crohn's disease, hepatitis, cirrhosis, hemorrhoids, systemic vasculitis, acquired immunodeficiency syndrome, gonorrhea, syphilis and chlamydia. (I) can be attached to a detectable label for use in diagnostics.

Dwg.0/8

TECH

UPTX: 20001010

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Peptide: (I) is 10, 15, 20, 25, 30, 35, 40, 45 or 50 residues in length, and further comprises a linking moiety, preferably SMTP, SPDP, LC-SPDP, Sulfo-LC-SDPD, SMCC, Sulfo-SMCC, MBS, Sulfo-MBS, SIAB, Sulfo-SIAB, SMPM, Sulfo-SMPB, EDC/Sulfo-NHS, or ABH, attached to the peptide. The linking moiety may be further attached to an agent, preferably a peptide, polypeptide, oligonucleotide, polynucleotide, detachable label or drug. The polypeptide is an enzyme, antibody region, region mediating protein-protein interaction, cytokine, growth factor, hormone, toxin, tumor suppressor, transcription factor, or apoptosis inducer. The polynucleotide encodes a polypeptide, a single chain antibody, an antisense construct or a ribozyme. The detectable label is rhodamine, fluorescein, green fluorescent protein or a radiolabel. The drug is an antibiotic, DNA damaging agent, enzyme inhibitor, or metabolite. Alternatively, (I) further comprises a non-pIgR targeting agent linked to the peptide. The targeting agent is an antigen binding domain of an antibody, a receptor ligand or ligand binding domain. (I) may comprise two pIgR-binding domains, and further comprise the linking agent and the agent.

Preferred Fusion Protein: The domain is Calpha3 domain. The non-antibody peptide or polypeptide is an enzyme, antibody region, region mediating protein-protein interaction, cytokine, growth factor, hormone, toxin, tumor suppressor, transcription factor, or apoptosis inducer.

Preferred Complex: The targeting complex further comprises a non-pIgR targeting agent.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Prior to performing the method of (5), the cell is transformed with an expression construct encoding pIgR under the control of a promoter.

Preparation: (I) can be produced by standard recombinant techniques.

L35 ANSWER 16 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-222357 [19] WPIDS
DNC C2000-067814
TI New dendritic polymer has a core containing a disulfide group, useful in diagnostics, drug delivery, gene therapy, magnetic resins imaging and in detection of ions and molecules.
DC A23 A26 A96 B04 D16 J04
IN BROTHERS, H M; CHENG, R C; HSU, Y; KLIMASH, J W; SPINDLER, R; SWANSON, D R; TOMALIA, D A; YIN, R
PA (DEND-N) DENDRITECH INC

CYC 1
 PI US 6020457 A 20000201 (200019)* 42p
 ADT US 6020457 A Provisional US 1996-24734P 19960930, US 1997-941527 19970930
 PRAI US 1996-24734P 19960930; US 1997-941527 19970930
 AB US 6020457 A UPAB: 20000419
 NOVELTY - A dendritic polymer (I) with a core containing a disulfide group and at least two dendrons emanating from the core, each dendron having at least two terminal groups, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a thin film coated substrate (II) comprising a substrate which has been subjected to application of ions or ionizable compounds of the same charge over its surface and one or more layers of organic materials which in each layer contains ions of the same charge, the ions of the layer immediately adjacent to the substrate have the opposite charge to the modified substrate and each further layer has a charge opposite that of the previous layer and at least one of the layers comprises a dendritic polymer;

(2) a quartz crystal electrode comprising a metal coated quartz crystal electrode coated with a dendritic polymer;

(3) a differentiated dendritic polymer (III) having a core with a disulfide group and at least 2 dendrons with at least 2 terminal groups emanating from the core where at least one of the dendrons has terminal groups which are different from those of the other dendron;

(4) a method (A) of making (I) comprising reacting the terminal groups of the core molecule with the dendrons so the single reactive groups present on the dendrons bond to one of the terminal reactive groups of the core molecule;

(5) a method (B) of making (II) comprising applying one or more layers of organic molecules from a solution to the substrate to be coated;

(6) a method (C) of making (III) comprising providing first and second dendritic polymers (I), combining and subjecting the first and second polymers to reducing conditions to form a mixture of two different types of (I) each having a single reactive sulfhydryl group and subjecting the mixture to aerobic, oxidizing conditions to form a mixture containing the first and second polymers and a differentiated dendritic polymer comprised of a part of each of the original first and second polymers;

(7) a gel (IV) comprised of **crosslinked** dendritic polymers which have sulfhydryl terminal groups that react with sulfhydryl terminal groups of another dendritic polymer to form a **crosslinked** gel; and

(8) a dendritic polymer conjugate (V) comprising a dendritic polymer which has a sulfhydryl group and a first carried material which has a sulfhydryl-reactive group, conjugated to the polymer at the sulfhydryl group.

USE - The dendritic polymers are useful in diagnostics, drug delivery, gene therapy, magnetic resins imaging and in detection of ions and molecules.

Dwg.0/26

TECH UPTX: 20000419

TECHNOLOGY FOCUS - POLYMERS - Preferred Core: The core is a polyamine compound containing a disulfide group. The polyamine compound is preferably a diamine, especially cystamine.

Preferred Dendrons: The dendrons are polyamidoamine dendrons. Each of the dendrons has branch arms which include a disulfide group which is inert under non-reducing conditions but which will react with a reducing agent to form a dendritic polymer having sulfhydryl terminal groups. The disulfide groups comprise the terminal groups of the branch arms. The differentiated dendritic polymer has at least one of the dendrons with terminal groups different from those of the other dendron, the first

dendron is of a different generation to the second dendron.

Preferred Method (A): The terminal groups of the core molecule are reacted with a first reagent to form a -one half generation dendrimer. Each molecule of the reagent has at least a single reactive site which bonds with one of the reactive terminal groups of the core molecule and at least one reactive group which becomes a terminal reactive group on the -one half generation dendrimer. Each of the terminal reactive groups on the -one half generation dendrimer are reacted with a second reagent to form a zero generation dendrimer. Each molecule of the second reagent includes at least one reactive site which bonds with a terminal reactive group on the -one half generation dendrimer and at least one reactive site which becomes a terminal reactive group on the zero generation dendrimer. Additional reagents can be employed to synthesize a dendritic polymer of a desired generation. An iterative excess reagent technique, alternately employing excess amounts of methyl acrylate and ethylene diamine can be used.

Preferred Electrode: The polymer coating of the quartz crystal electrode comprises a monolayer of dendritic polymer molecules.

Preferred Gel: (IV) comprises dendritic polymers which have **amine terminal groups** and iminothiolane, preferably a polyamidoamine dendrimer, and are prepared by subjecting a dendritic polymer with **sulfide groups** to oxidizing conditions. (IV) can be resolubilized by adding a reducing agent such as dithioreitol to provide a redox reversible gel.

Preferred Carried Materials: (V) includes surface functional groups with a second carried material **conjugated** to them. At least one of the first and second carried materials is a bioactive agent which is a pharmaceutical agent, drug, pharmaceutical intermediary, radioprotective agent, toxin, antibody, antibody fragment, hormone, biological responses modifier, scavenging agent, **polypeptide** and/or **protein**.

. Preferably at least one of the first and second carried materials is an **oligonucleotide**. The 'second carried material' is a bioactive agent and/or a signal amplifier and is preferably triethyltinpropanate.

L35 ANSWER 17 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 1999-633734 [54] WPIDS
 CR 1999-602308 [52]
 DNN N1999-467958 DNC C1999-185059
 TI Compositions of matter comprising photoluminescent compound, have
 excitation and emission spectra in inaccessible regions of spectrum e.g.
 red and near infrared.
 DC B02 B04 D16 E24 G04 J04 S03
 IN TERPETSCHNIG, E A; OSWALD, B; PATSENKER, L D
 PA (TERP-I) TERPETSCHNIG E A
 CYC 87
 PI WO 9951702 A1 19991014 (199954)* EN 80p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ UG ZW
 W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
 GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
 LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
 TT UA UG US UZ VN YU ZA ZW
 AU 9933863 A 19991025 (200011)
 EP 1078023 A1 20010228 (200113) EN
 R: AT BE CH DE DK ES FI FR GB IE IT LI LU NL SE
 US 6538129 B1 20030325 (200325)
 ADT WO 9951702 A1 WO 1999-US7627 19990407; AU 9933863 A AU 1999-33863
 19990407; EP 1078023 A1 EP 1999-915319 19990407, WO 1999-US7627 19990407;
 US 6538129 B1 Cont of WO 1999-US7627 19990407, US 2000-684627 20001006
 FDT AU 9933863 A Based on WO 9951702; EP 1078023 A1 Based on WO 9951702

PRAI US 1998-83820P 19980501; DE 1998-19815659 19980408; US 2000-684627
20001006

AB WO 9951702 A UPAB: 20030516

NOVELTY - Compositions of matter comprising photoluminescent compound.

DETAILED DESCRIPTION - Photoluminescent compound is of formula (I):
Z = 4-6-membered aromatic ring; A-F are substituents of Z, F = absent when
Z = 5-membered ring and E, F are absent when Z = 4-membered ring; A-F may
be present in any order provided that B and C are adjacent, in which case
A, D-F is neutral or provided that B and C are separated by one of A, D-F
in which case one of A, D-F is negatively charged; A = S, Se, Te or
C(Ra)(R); and B, C = W1, W2. Full definitions are provided in the
Definitions (Full definitions) Field. INDEPENDENT CLAIMS are also
included for (1) method of performing photoluminescence assay; and (2)
method of synthesizing photoluminescent compounds.

USE - Used to perform photoluminescence assays (claimed). Used in
spectroscopy, microscopy, immunoassays and hybridization assays, in free
and **conjugated** forms as probes, labels and indicators, in
competitive assays that include recognition groups, binding partners or
analytes such as biomolecules, polymers and drugs, in immunoassays such as
sandwich assays using secondary antibodies, binding between avidin and
biotin, **protein A** and immunoglobulins, lectins and sugars
(concanavalin A and glucose), to sequence nucleic acids and
peptides, e.g. to trace **DNA** fragments, for fluorescence
in situ hybridization methods, for single nucleotide applications and for
screening assays for combinatorial libraries of compounds.

ADVANTAGE - Have excitation and emission spectra in relatively
inaccessible regions of spectrum including red and near infrared.
Multicolor labeling allows different biochemical parameters to be
monitored simultaneously.

DESCRIPTION OF DRAWING(S) - Excitation (dotted line) and emission
(solid line) spectra for (13)-human serum albumin (HAS) in phosphate
buffered saline.

Dwg.1/1

TECH

UPTX: 19991221

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred compositions -
Compositions further comprise carrier associated non-covalently with the
photoluminescent compound or covalently through reaction with a reactive
group on at least one Z. Compositions further comprise luminophores or
chromophores. One of the photoluminescent compound and second compound is
an energy transfer donor and the other is an energy transfer acceptor.
Preferred photoluminescent compound - Z is based on squaric acid, croconic
acid or rhodizonic acid. At least one of Z = reactive group, preferably
chosen for reacting with **amine groups**
(N-hydroxysuccinimide esters, isothiocyanates or sulfonylhalogenides),
thio groups (iodoacetamides or maleimides) or nucleic
acids (phosphoramidites) or = **linked** carrier, preferably
polypeptide, polynucleotide, bead, microplate well surface or
other solid surface. At least one substituent of Z is an ionic substituent
capable of increasing the hydrophilicity of the entire photoluminescent
compound, preferably SO₃⁻, COO⁻ or n(RI)⁺ (RI = aliphatic or aromatic
group). Photoluminescent compound is suitable for excitation in the red or
near infrared range. Photoluminescent compound is capable of emitting
light with wavelength of 600-900 nm. Photoluminescent compound has a
Stokes' shift of at least about 5 nm. Photoluminescent compound is capable
of covalently reacting with biological cells, **DNA**, lipids,
nucleotides, polymers, **proteins** and/or pharmacological agents.
Photoluminescent compound is asymmetric or symmetric about Z.
Photoluminescent compound may be induced to luminesce by exposing it to
electromagnetic, chemical and or electrochemical energy.

L35 ANSWER 18 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-430042 [36] WPIDS
DNC C1999-126684
TI Determining sequence of a nucleic acid by mass spectrometry.
DC B04 C06 D16 J04
IN CANTOR, C; KANG, C; KIM, Y T; KOESTER, H; KWON, Y; LITTLE, D P; LOUGH, D
M; O'DONNELL, M J; XIANG, G; CANTOR, C R; KIM, Y; O'DONNELL, M J; LITTLE, M
J
PA (KOAD) KOREA ADV INST SCI & TECHNOLOGY; (ODON-I) O'DONNELL M J; (SEQU-N)
SEQUENOM INC
CYC 85
PI WO 9931278 A1 19990624 (199936)* EN 116p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
UA UG US UZ VN YU ZW
AU 9919187 A 19990705 (199948)
EP 1038031 A1 20000927 (200048) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
NO 2000003058 A 20000815 (200052)
US 6268131 B1 20010731 (200146)
KR 2001033130 A 20010425 (200164)
JP 2002508192 W 20020319 (200222) 159p
AU 745149 B 20020314 (200231)
JP 3331210 B2 20021007 (200273) 50p
EP 1038031 B1 20031126 (200402) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
DE 69820111 E 20040108 (200411)
ADT WO 9931278 A1 WO 1998-US26718 19981215; AU 9919187 A AU 1999-19187
19981215; EP 1038031 A1 EP 1998-963969 19981215, WO 1998-US26718 19981215;
NO 2000003058 A WO 1998-US26718 19981215, NO 2000-3058 20000614; US
6268131 B1 US 1997-990851 19971215; KR 2001033130 A KR 2000-706503
20000614; JP 2002508192 W WO 1998-US26718 19981215, JP 2000-539175
19981215; AU 745149 B AU 1999-19187 19981215; JP 3331210 B2 WO
1998-US26718 19981215, JP 2000-539175 19981215; EP 1038031 B1 EP
1998-963969 19981215, WO 1998-US26718 19981215; DE 69820111 E DE
1998-620111 19981215, EP 1998-963969 19981215, WO 1998-US26718 19981215
FDT AU 9919187 A Based on WO 9931278; EP 1038031 A1 Based on WO 9931278; JP
2002508192 W Based on WO 9931278; AU 745149 B Previous Publ. AU 9919187,
Based on WO 9931278; JP 3331210 B2 Previous Publ. JP 200208192, Based on
WO 9931278; EP 1038031 B1 Based on WO 9931278; DE 69820111 E Based on EP
1038031, Based on WO 9931278
PRAI US 1997-990851 19971215
AB WO 9931278 A UPAB: 19990908
NOVELTY - A new method for determining the sequence of a target nucleic
acid molecule comprises transcribing the nucleic acid molecule which has a
promoter, followed by determining the molecular weight of the transcripts
by mass spectrometry.
DETAILED DESCRIPTION - A new method for determining the sequence of a
target nucleic acid molecule comprises:
(a) providing a nucleic acid molecule comprising a promoter and
target nucleic acid sequence operatively **linked** to the promoter,
where the nucleic acid molecule is immobilized on a solid support;
(b) transcribing the promoter-containing nucleic acid molecule with
an RNA polymerase that recognizes the promoter under conditions where a
nested set of RNA transcripts from the target is produced; and

(c) determining the molecular weight of the transcripts by mass spectrometry and therefore determining the nucleic acid sequence of the target molecule.

An INDEPENDENT CLAIM is also included for a method of identifying transcriptional terminator or attenuator sequences comprising:

(a) immobilizing a nucleic acid promoter containing probe on a solid support, where the nucleic acid promoter containing probe comprises at least 5 nucleotides at the X-end of the coding strand that is complementary to a single stranded region at the X-end of the target nucleic acid;

(b) hybridizing the nucleic acid to be sequenced to the immobilized nucleic acid probe;

(c) transcribing the target nucleic acid with an RNA polymerase to produce a sequence-terminated RNA transcript, where the RNA polymerase recognizes the promoter; and

(d) determining the molecular weight value of the RNA transcript by mass spectrometry, where the terminator sequence or attenuator is identified.

USE - The method is used for sequencing nucleic acids by mass spectrometry. In particular, the method can be used to identify transcriptional terminator or attenuator sequences (claimed). Rho-dependent and rho-independent terminators may be detected by the method.

ADVANTAGE - The array format comprising high densities of nucleic acid probes facilitates mass spectrometric detection. RNA fragments are more stable during matrix-assisted laser desorption/ionization (MALDI) mass spectrometry than DNA fragments. This may be a result of the 2'-hydroxyl group on the sugar moiety of RNA, which helps to reduce depurination during the MALDI process. Ribonucleoside triphosphate analogues are used in the method, so that the resulting RNA transcripts have reduced secondary structure, or the fidelity of termination and turnover of the RNA polymerase enzyme is increased compared to RNA transcripts formed from ribonucleoside triphosphates.

Dwg.0/17

TECH

UPTX: 19990908

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The promoter-containing nucleic acid molecule is immobilized by the 5' end of the coding strand or the 3' end of the non-coding strand. The nucleic acid is DNA or peptide nucleic acid (PNA). The nucleic acid molecule comprising a promoter and target is prepared by hybridizing a promoter-containing probe having a coding and non-coding strand to a nucleic acid molecule comprising a target sequence, where hybridization occurs between a single-stranded region of the promoter-containing probe and a complementary single-stranded region at one end of the molecule comprising the target. The target is single-stranded and the complementary sequence is at the 3' end. The double-stranded promoter-containing probe comprises a single-stranded region of at least 5 nucleotides at the 3' end of the coding strand that are complementary to the corresponding target sequence.

Alternatively, the target is double-stranded except for an at least 5 contiguous nucleotide single-stranded region that is complementary to the corresponding portion of the probe and the single-stranded portion of the promoter containing molecule is at the same end, relative to the promoter, such that the single-stranded region is on the target containing molecule. The promoter containing molecule is immobilized on the solid support prior to hybridization of the target containing molecule. Alternatively, the hybridization may be performed prior to immobilization of the promoter containing molecule on the solid support.

Nicks in the resulting molecules are ligated prior to transcription by the RNA polymerase. RNA polymerase is used to transcribe the promoter-target

nucleic acid to produce several base-specifically-terminated RNA transcripts. The RNA transcripts may be specifically cleaved with base-specific ribonucleases to produce a set of cleaved fragments whose weight values are assessed by mass spectrometry. The sequence of all or a part of the target is determined by the RNA transcripts according to the molecular weight. The nucleic acid molecule comprising the promoter is produced by immobilizing a single-stranded molecule that comprises a promoter or the complement of a promoter and hybridizing a fragment that comprises its complement, where the resulting molecule comprises a double-stranded region containing a promoter and a single-stranded portion of at least 5 nucleotides. The promoter is an archaeobacteria, eubacteria, bacteriophages, DNA viruses, RNA viruses, plants, plant viruses or animal promoters.

Hybridization of the target and promoter-containing molecules results in the formation of a nick in the coding strand corresponding to positions beyond +6 relative to the start of transcription from the promoter. The nick is preferably at position +7, +8, +9 or +19 positions.

Prior to immobilization of the nucleic acid, the surface of the support is derivatized, by reaction of the surface with an aminosilane, e.g.

3-aminopropyltriethoxysilane, to produce primary amines on the surface of the support. The primary amines are further reacted with a thiol-reactive cross-linking reagent, e.g. N-succinimidyl (4-iodoacetyl) aminobenzoate (SIAB), to form a thiol-reactive solid support.

Immobilization of the nucleic acid probe to a solid support is effected by reacting the thiol reactive solid support with a nucleic acid probe having a free 5'- or 3'-thiol group. The nucleic acid is immobilized to the surface at a density of at least 20 fmol/mm² by a covalent linkage.

The nucleic acids are immobilized on the surface of a solid support (e.g. silicon or silicon coated) in the form of an array. The solid surface has many wells which are pitted.

Transcription reactions are performed in the presence of a ribonucleoside triphosphate analogue, where the resulting RNA transcripts have reduced secondary structure, or the fidelity of termination and turnover of the RNA polymerase enzyme is increased compared to RNA transcripts formed from ribonucleoside triphosphates. The analogues are chosen from inosine 5'-triphosphate (ITP), 4-thiouridine 5'-triphosphate (UTP), 5-bromo UTP and 5'-iodo CTP.

Transcription may be performed in the presence of one or more 3'-deoxyribonucleotides. The nucleic acid may be immobilized to the solid support via a linker. The linkage is photolabile, acid labile or chemically cleavable. A matrix material is added to the surface of the support before or after immobilization of the nucleic acid for mass spectrometry. RNA transcripts are conditioned prior to performing mass spectrometry. The RNA polymerase is a DNA-dependent or RNA-dependent RNA polymerase. The RNA polymerase is especially that of Escherichia coli, T7, SP6 or T3 RNA polymerase or Qbeta replicase.

L35 ANSWER 19 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 1999-190636 [16] WPIDS

DNN N1999-139408 DNC C1999-056165

TI Detection and identification of micro-organisms - by in situ staining with a composition which degrades the cell wall to allow penetration of a probe.

DC B04 C07 D15 D16 D21 J04 S03

IN SCHUT, F; TAN, P S T

PA (MICR-N) MICROSCREEN-BV

CYC 83

PI WO 9910533 A1 19990304 (199916)* EN 70p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG
MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG
US UZ VN YU ZW

AU 9888904 A 19990316 (199930)

EP 1009862 A1 20000621 (200033) EN

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

ADT WO 9910533 A1 WO 1998-NL481 19980826; AU 9888904 A AU 1998-88904 19980826;

EP 1009862 A1 EP 1998-940684 19980826, WO 1998-NL481 19980826

FDT AU 9888904 A Based on WO 9910533; EP 1009862 A1 Based on WO 9910533

PRAI EP 1997-202618 19970826

AB WO 9910533 A UPAB: 19990424

NOVELTY - Detecting and identifying micro-organisms by staining with a composition that partly degrades the cell wall or cell membrane of the micro-organism, so that a probe can penetrate the cell, is new. The probe is targeted to a sequence in the micro-organism, and is subsequently detected.

DETAILED DESCRIPTION - A method for in situ staining of micro-organisms (e.g. viruses, bacteria, yeast fungi and plant cells) comprises: (a) mixing a material containing at least one micro-organism with a composition which can (partly) degrade a cell wall or cell membrane of a micro-organism thereby allowing for penetration through the wall or membrane of a (labelled) probe; (b) reacting the probe with an antigen or nucleic acid molecule present in the cell; and (c) detecting the presence of the probe in the micro-organism. The micro-organism is optionally fixed with a fixative to further retain its corpuscular character.

INDEPENDENT CLAIMS are also included for the following: (1) a nucleic acid probe derived from a thiolated probe **linked** to horse-radish peroxidase with a sulfo-**SMCC linker**; (2) a method for **linking** a nucleic acid probe to horse-radish peroxidase (HRP), comprising mixing a thiol **oligonucleotide** with a **SMCC-HRP** complex, incubating the mixture, and purifying the probe by ultrafiltration; (3) a diagnostic test kit for use with in situ staining which comprises a cell wall degrading composition and a nucleic acid probe; and (4) an enzyme-**linked** assay or diagnostic kit which comprises the probe defined in (1).

USE - The method can be used for identification of organisms, and possibly to differentiate between strains, e.g. in cheese-making. It can also be used to measure the potential metabolic activity or level of individual enzymes. The method can be used to study mRNA activity in, e.g. fermentation cultures. The method can also be used to study the effect of novel foods, probiotics, and functional foods on intestinal microflora, to monitor the development of mixed bacterial populations in fermentation processes, e.g. cheese and other dairy fermentation, beer, wine, etc., as well as in modern biotechnology, to identify and quantify the presence and activity of micro-organisms in wastewater treatment systems and bioremediation processes, to determine the microbial status of (polluted) soils, waters, gases, potable water, swimming water and surface water. The method can also be used to detect pathogens and bacterial resistance, especially 'carries-carrying' oral Streptococci for the toothpaste industry, and Mycobacterium tuberculosis directly in sputum samples, which cannot be detected in situ by conventional in situ fluorescence techniques.

ADVANTAGE - The method allows for controlled degradation of cell walls in combination with a detection technique, allowing for in situ staining and detection. The present method provides a signal amplification of at least 30-50 fold, and even 80 fold, as compared with conventional fluorescent probes. The method utilises short probes, instead of the long (approximately 200 bp) labelled transcripts presently used for in situ mRNA detection. The method allows direct detection of non-growing cells,

and for cells which contain low copy numbers of mRNA.
Dwg.0/8

L35 ANSWER 20 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-105092 [09] WPIDS
DNN N1999-075937 DNC C1999-031144
TI New plasmid expressing fusion protein of polypeptide and methylase - binds to methylase binding site in the plasmid forming a covalent **conjugate**, used to create libraries for screening, or in vitro evolution, of mutant peptides with altered binding properties.
DC B04 D16 S03
IN EPSTEIN, D M
PA (SCRI) SCRIPPS RES INST
CYC 1
PI US 5856090 A 19990105 (199909)* 90p
ADT US 5856090 A US 1994-305764 19940909
PRAI US 1994-305764 19940909
AB US 5856090 A UPAB: 19990302

New plasmid (A) comprises: (a) gene fusion construct (GFC) including a gene (I) for cytosine (C5) **DNA** methylase (II) covalently attached, directly or through a **linker**, to a gene (III) encoding a **polypeptide** determinant (IV), with GFC expressing a fusion of (II) and (IV); (b) a promoter operatively **linked** to the gene fusion construct for transcription of GFC to mRNA; and (c) a methylase **conjugation** element (MCE) **linked** to GFC, directly or through a **linker**, containing a methylase binding site (**MBS**) including at least one copy of a nucleotide sequence (NS) that includes a cytidine suicide analogue (CSA) binding irreversibly to and being a methylase substrate for (II) of the fusion **protein**. Also claimed are: (1) plasmid-**polypeptide** determinant **conjugates** (PPDC) consisting of (A) covalently coupled to the fusion **protein** from GFC via a pyrimidine group of CSA; (2) libraries of PPDC; and (3) methods for obtaining a nucleic acid sequence (IIIa) encoding a **polypeptide** (IVa) that is an altered form of wild-type (IV), using the libraries of (2).

USE - The method can be used to identify mutants of glutathione-S-transferase (GST), an important target in treatment of cancer and Schistosoma infection and can also be applied to hormones or enzymes. The method can be used to isolate low copy number wild-type proteins, provided a specific binding agent is available. The identified mutants can then be used to screen inhibitors and inactivators (potential anti-neoplastic and antimalarial agents) for their binding affinity.

ADVANTAGE - The method rapidly and efficiently **links** genetic information with the encoded protein, making repeated rounds of screening without use of a phage-display library possible. Since PPDC are covalently **linked**, they are stable, easily manipulated (e.g. affinity chromatography can be done without breaking the **link**) and are compatible with nucleic acid sequencing and amplification techniques.

Dwg.0/24

L35 ANSWER 21 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1998-216491 [19] WPIDS
DNC C1998-068600
TI Sequence independent amplification of **DNA** - without the need for prior sequence knowledge or requirements.
DC B04 D16
IN BOHLANDER, S K
PA (ARCH-N) ARCH DEV CORP
CYC 1

PI US 5731171 A 19980324 (199819)* EN 26p
 ADT US 5731171 A US 1993-96637 19930723
 PRAI US 1993-96637 19930723
 AB US 5731171 A UPAB: 19980512

A method for the sequence independent amplification (SIA) of DNA is new. This comprises:

(a) denaturing a DNA sample and annealing it with a first primer (I) which has a random 3' sequence and defined 5' sequence;

(b) incubating the DNA-primer hybrid with a DNA polymerase, especially T7 DNA polymerase, to synthesise a product; and

(c) carrying out a low stringency, then a high stringency Polymerase Chain Reaction (PCR) on the product using a second primer (II) that has the same 3' as the first, but also has an additional 5' overhang.

USE - The method is useful for amplifying small amounts of microdissected chromosomal samples (yeast artificial chromosome (YAC), gel purified, genomic or cloned DNA) which do not contain any particular restriction sites or repetitive sequences and can be derived from any species or organism. The method can also be used for deriving fluorescent in situ hybridisation (FISH) labelled products which can be used to screen YACs for chromosomal translocations in human tumours.

ADVANTAGE - This method does not require any prior sample sequence knowledge. Also no prior restriction enzyme manipulation and linker attachment to isolate unknown sequences is required. Screening of chromosomal translocations is simplified as several reactions can be run at the same time and the chance of contamination is cut down as the number of steps and manipulations is reduced.
 Dwg.0/7

L35 ANSWER 22 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 1994-279761 [34] WPIDS
 DNC C1994-127735

TI Photo-protein binding reagent **conjugate** compsn. useful in diagnostic and detection assays - comprises luminescent, sulphhydryl-activated photo-protein coupled to sulphhydryl-reactive binder.

DC B04 D16

IN STULTS, N L

PA (SEAL-N) SEALITE SCI INC

CYC 48

PI WO 9418342 A1 19940818 (199434)* 32p
 RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
 W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB HU JP KP KR KZ LK LU
 LV MG MN MW NL NO NZ PL PT RO RU SD SE SK UA VN

AU 9461718 A 19940829 (199501)

EP 683822 A1 19951129 (199601) EN

R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

US 5486455 A 19960123 (199610) 15p

JP 08506897 W 19960723 (199650) 38p

EP 683822 A4 19971105 (199840)

IL 108607 A 19981206 (199913)

EP 683822 B1 20020502 (200230) EN

R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

DE 69430523 E 20020606 (200245)

ADT WO 9418342 A1 WO 1994-US1387 19940204; AU 9461718 A AU 1994-61718 19940204, WO 1994-US1387 19940204; EP 683822 A1 EP 1994-908734 19940204, WO 1994-US1387 19940204; US 5486455 A Cont of US 1993-17116 19930212, US 1994-293648 19940822; JP 08506897 W JP 1994-518303 19940204, WO 1994-US1387 19940204; EP 683822 A4 EP 1994-908734 19940204; IL 108607 A IL 1994-108607 19940209; EP 683822 B1 EP 1994-908734 19940204, WO 1994-US1387 19940204; DE 69430523 E DE 1994-630523 19940204, EP 1994-908734 19940204,

WO 1994-US1387 19940204

FDT AU 9461718 A Based on WO 9418342; EP 683822 A1 Based on WO 9418342; JP
08506897 W Based on WO 9418342; EP 683822 B1 Based on WO 9418342; DE
69430523 E Based on EP 683822, Based on WO 9418342

PRAI US 1993-17116 19930212; US 1994-293648 19940822

AB WO 9418342 A UPAB: 19971006

Photoprotein binding reagent **conjugate** comprises a sulphydryl
activated photoprotein capable of participating in luminescent reaction to
produce light, copuled to sulphydryl reactive binding reagent capable of
binding specifically to analyte.

Also claimed is preparation of a photoprotein-binding reagent
conjugate compsn. by coupling sulphydryl-activated photoprotein
capable of participating in a luminescent reaction space to produce light,
to sulphydryl-reactive binding reagent capable of binding specifically to
analyte.

Conjugates are pref. (1) photoprotein selected from
aopaequorin, aequorin, apo-obelin, obelin, apo-mnemiopsin, mnemiopsin,
apo-berovin, berovin, pholasin, luciferases, bioluminescent
proteins from Pelagia, or ostracods; and (2) binding reagent
selected from streptavidin/avidin, lectins, enzymes, glycoproteins,
peptides, hormones, receptors, antigens, drugs, antibodies and
antigen binding fragments thereof, RNA, **DNA** and
oligonucleotides.

USE - Presence or amount of analyte in sample can be determined by
using photoprotein-binding reagent **conjugate** in binding assay
(claimed).

Dwg.0/6

=>

=> fil caplus

FILE 'CAPLUS' ENTERED AT 15:12:56 ON 26 FEB 2004

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FILE COVERS 1907 - 26 Feb 2004 VOL 140 ISS 9

FILE LAST UPDATED: 25 Feb 2004 (20040225/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que l31

L1	(3)SEA FILE=REGISTRY ABB=ON PLU=ON	103708-62-3 OR 215312-86-0 OR 185332-92-7 OR 92921-25-0
L2	(6)SEA FILE=REGISTRY ABB=ON PLU=ON	L1 OR 103708-09-4 OR 106145-13-5 OR 92921-26-1
L3	(7)SEA FILE=REGISTRY ABB=ON PLU=ON	L2 OR 343934-41-8
L4	(25)SEA FILE=REGISTRY ABB=ON PLU=ON	PHENYL (L) ISOPROPYL (L) ADENOSINE
L5	(5)SEA FILE=REGISTRY ABB=ON PLU=ON	L4 AND N6
L6	(3)SEA FILE=REGISTRY ABB=ON PLU=ON	C19H23N5O4 AND L5
L7	(10)SEA FILE=REGISTRY ABB=ON PLU=ON	L6 OR L3
L8	(7)SEA FILE=REGISTRY ABB=ON PLU=ON	L7 NOT L6
L9		8 SEA FILE=REGISTRY ABB=ON PLU=ON	L8 OR 31252-85-4
L10		104 SEA FILE=CAPLUS ABB=ON PLU=ON	SULFO (2W) (SMCC OR EMCS OR GMBS OR KMUS OR MBS OR SIAB OR SMPB OR LC SMPT OR SVSB OR SIACX OR SIA OR SIAXX OR NPJA)
L11		247 SEA FILE=CAPLUS ABB=ON PLU=ON	L9 OR L10
L12		630930 SEA FILE=CAPLUS ABB=ON PLU=ON	OLIGONUCLEOTIDE#/OBI OR NUCLEOTIDE?/OBI OR DNA/OBI
L13		1270374 SEA FILE=CAPLUS ABB=ON PLU=ON	PROTEIN#/OBI
L14		135497 SEA FILE=CAPLUS ABB=ON PLU=ON	L12 (L) L13
L15		693 SEA FILE=CAPLUS ABB=ON PLU=ON	L14 (L) CONJUGAT?/OBI
L18		4 SEA FILE=CAPLUS ABB=ON PLU=ON	L15 AND L11
L19		53407 SEA FILE=CAPLUS ABB=ON PLU=ON	(AMINO OR AMINE OR NH2) (S) (?NUCLEOTIDE? OR DNA)
L20		1037 SEA FILE=CAPLUS ABB=ON PLU=ON	L19 (S) MODIF?
L21		6 SEA FILE=CAPLUS ABB=ON PLU=ON	L20 AND L15
L22		198 SEA FILE=CAPLUS ABB=ON PLU=ON	L14 AND L20
L23		1 SEA FILE=CAPLUS ABB=ON PLU=ON	L22 AND L11
L24		114 SEA FILE=CAPLUS ABB=ON PLU=ON	L19 AND L15
L25		15 SEA FILE=CAPLUS ABB=ON PLU=ON	L24 AND (THIO# OR SULF?)
L26		23 SEA FILE=CAPLUS ABB=ON PLU=ON	L25 OR L23 OR L21 OR L18
L27		63 SEA FILE=CAPLUS ABB=ON PLU=ON	L11 AND L12
L28		31 SEA FILE=CAPLUS ABB=ON PLU=ON	L27 AND L13
L29		24 SEA FILE=CAPLUS ABB=ON PLU=ON	L28 AND ?LINK?
L30		13 SEA FILE=CAPLUS ABB=ON PLU=ON	L29 AND CONJUG?

L31 34 SEA FILE=CAPLUS ABB=ON PLU=ON L30 OR L26

=> d .ca l31 1-34

L31 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2003:836754 CAPLUS
 DOCUMENT NUMBER: 139:341721
 TITLE: Histone **conjugates** for delivery of drugs to cell nuclei
 INVENTOR(S): Gilon, Chaim; Loyter, Abraham; Graessman, Adolf; Sperling, Joseph; Hariton-Gazal, Ilana
 PATENT ASSIGNEE(S): Yisum Research Development Company of the Hebrew University of Jerusalem, Israel; Yeda Research and Development Co., Ltd.
 SOURCE: PCT Int. Appl., 88 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086273	A2	20031023	WO 2003-IL279	20030403
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2002-370221P P 20020408
 US 2002-429575P P 20021129

AB A **conjugate** of a histone moiety covalently attached to a macromol.-of-interest, in which the histone moiety is transportable through the cell membrane and importable into the cell nuclei, is disclosed. Further disclosed are chemical and recombinant methods of preparing such a **conjugate**, pharmaceutical compns. containing same and uses thereof for delivering therapeutically active macromols. into cells. A novel method for quant. determining a cytoplasmic uptake and/or a nuclear uptake of a moiety into cells is also disclosed.

IC ICM A61K

CC 63-5 (Pharmaceuticals)

ST cell nucleus drug delivery histone **conjugate**

IT Histones

RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (H1, **conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)

IT Histones

RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

- (H2A, **conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)
- IT Histones
 RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (H2B, **conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)
- IT Histones
 RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (H3, **conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)
- IT Histones
 RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (H4, **conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)
- IT Spheres
 (beads; histone **conjugates** for delivery of drugs to cell nuclei)
- IT Drug delivery systems
 (carriers; histone **conjugates** for delivery of drugs to cell nuclei)
- IT Enzymes, uses
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (colorimetric reagents; histone **conjugates** for delivery of drugs to cell nuclei)
- IT Histones
 RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)
- IT DNA
 Gene, animal
 Nucleic acids
 Oligonucleotides
 Proteins
 RNA
 RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)
- IT Animal tissue culture
 Cell nucleus
 Fluorescent substances
 Linking agents
 Microarray technology
 Microtiter plates
 Pigments, nonbiological
 Sulfhydryl group
 (histone **conjugates** for delivery of drugs to cell nuclei)
- IT Glass, uses
 RL: NUU (Other use, unclassified); USES (Uses)
 (histone **conjugates** for delivery of drugs to cell nuclei)
- IT Lymphocyte

(human; histone **conjugates** for delivery of drugs to cell nuclei)

IT Biological transport
(import; histone **conjugates** for delivery of drugs to cell nuclei)

IT Biological transport
(intracellular; histone **conjugates** for delivery of drugs to cell nuclei)

IT Human
(lymphocytes of; histone **conjugates** for delivery of drugs to cell nuclei)

IT Drug delivery systems
(targeted; histone **conjugates** for delivery of drugs to cell nuclei)

IT 103708-09-4, Sulfo-smcc
RL: RCT (Reactant); RACT (Reactant or reagent)
(**crosslinking** agent; histone **conjugates** for delivery of drugs to cell nuclei)

IT 58-85-5, Biotin
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(histone **conjugates** for delivery of drugs to cell nuclei)

IT 393511-86-9P 524943-98-4P
RL: PNU (Preparation, unclassified); PRP (Properties); PREP (Preparation)
(histone **conjugates** for delivery of drugs to cell nuclei)

L31 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:738727 CAPLUS

DOCUMENT NUMBER: 139:288452

TITLE: Electrogenated chemiluminescence. 72. Determination of immobilized DNA and C-reactive protein on Au(111) electrodes using tris(2,2'-bipyridyl)ruthenium(II) labels

AUTHOR(S): Miao, Wujian; Bard, Allen J.

CORPORATE SOURCE: Department of Chemistry and Biochemistry, The University of Texas at Austin, Austin, TX, 78712-0165, USA

SOURCE: Analytical Chemistry (2003), 75(21), 5825-5834

CODEN: ANCHAM; ISSN: 0003-2700

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Anodic electrogenerated chemiluminescence (ECL) with tri-n-propylamine (TPRA) as a coreactant was used to determine DNA and C-reactive protein (CRP) by immobilizations on Au(111) electrodes using tris(2,2'-bipyridyl)ruthenium(II) (Ru(bpy)₃²⁺) labels. A 23-mer synthetic single-stranded (ss) DNA derived from the Bacillus anthracis with an **amino-modified** group at the 5' end position was covalently attached to the Au(111) substrate precoated with a self-assembled **thiol** monolayer of 3-mercaptopropanoic acid (3-MPA) in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDAC) and then hybridized with a target ssDNA tagged with Ru(bpy)₃²⁺ ECL labels. Similarly, biotinylated anti-CRP species were immobilized effectively onto the Au(111) substrate precovered with a layer of avidin linked covalently via the reaction between avidin and a mixed **thiol** monolayer of 3-MPA and 16-mercaptohexadecanoic acid on Au(111) in the presence of EDAC and N-hydroxysuccinimide. CRP and anti-CRP tagged with Ru(bpy)₃²⁺ labels were then conjugated to the surface layer. ECL responses were generated from the modified electrodes described above by immersing them in a TPRA-containing electrolyte solution. A series of electrode treatments, including blocking free -COOH groups with ethanol

amine, pinhole blocking with bovine serum albumin, washing with EDTA/NaCl/Tris buffer, and spraying with inert gases, were used to reduce the nonspecific adsorption of the labeled species. The ECL peak intensity was linearly proportional to the analyte CRP concentration over the range 1-24 µg/mL. CRP concns. of two unknown human plasma/serum specimens were measured by the standard addition method based on this technique.

CC 9-7 (Biochemical Methods)

Section cross-reference(s): 4, 10

IT Avidins

RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(**conjugates**; electrogenerated chemiluminescence determination of immobilized **DNA** and C-reactive **protein** on Au(111) electrodes using tris(2,2'-bipyridyl)ruthenium(II) labels)

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:662897 CAPLUS

DOCUMENT NUMBER: 139:271618

TITLE: Affinity capture-facilitated preparation of aequorin-oligonucleotide conjugates for rapid hybridization assays

AUTHOR(S): Glynnou, Kyriaki; Ioannou, Penelope C.; Christopoulos, Theodore K.

CORPORATE SOURCE: Department of Chemistry, University of Athens, Athens, 15771, Greece

SOURCE: Bioconjugate Chemistry (2003), 14(5), 1024-1029
CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We report a general procedure for the preparation of biomol. conjugates that combine the mol. recognition properties of oligonucleotides with the high detectability of the photoprotein aequorin. Central to the conjugation protocols is the use of recombinant aequorin fused to a hexahistidine tag. In one protocol, an **amino-modified oligonucleotide** was treated with a homobifunctional cross-linker carrying two N-hydroxysuccinimide ester groups, and the derivative was allowed to react with (His)6-aequorin. A second strategy involved the introduction of protected **sulfhydryl** groups into (His)6-aequorin and subsequent reaction with a heterobifunctional linker containing a N-hydroxysuccinimide and a maleimide group. The strong, but reversible, binding of (His)6-aequorin to Ni²⁺-nitrilotriacetic acid agarose enabled the rapid and effective removal of the unreacted oligonucleotide, which otherwise diminishes the performance of the hybridization assay by competing with the conjugate for the complementary target sequence. Aequorin-oligo conjugates prepared by affinity capture showed similar performance with those purified by anion-exchange HPLC. The conjugates were applied to the development of rapid bioluminometric hybridization assays. The anal. range extended from 2 to 2000 pmol/L of target DNA. The reproducibility was less than 10%. The conjugate obtained from a reaction of 10 nmol of (His)6-aequorin is sufficient for about 5000 hybridization assays. The proposed conjugation strategy is general because a variety of reporter proteins can be fused to hexahistidine tag by using suitable vectors that are com. available.

CC 3-1 (Biochemical Genetics)

IT Oligodeoxyribonucleotides

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**amino-modified** conjugates with aequorin; affinity capture-facilitated preparation of aequorin-oligonucleotide

conjugates for rapid hybridization assays)

IT Aequorins
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (fusion **protein** with hexahistidine tag, **conjugates**
 with oligodeoxyribonucleotides; affinity capture-facilitated preparation of
 aequorin-**oligonucleotide conjugates** for rapid
 hybridization assays)

IT 139-13-9D, Nitrilotriacetic acid; Ni²⁺-salt; immobilized on agarose
 14701-22-5D, Ni²⁺, nitrilotriacetic acid-salt, biological studies
 64134-30-1D, Hexahistidine, fusion **protein** with aequorin
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (affinity capture-facilitated preparation of aequorin-
oligonucleotide conjugates for rapid hybridization
 assays)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2003:639033 CAPLUS
 DOCUMENT NUMBER: 139:193936
 TITLE: Methods for preparation of DNA or protein microarrays
 and their use in diagnosis of disease
 INVENTOR(S): Nasso, Pierre; Potier, Marie Claude; Talini, Luc;
 Gibelin, Nathalie; Rossier, Jean
 PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique CNRS,
 Fr.; Institut Curie
 SOURCE: Fr. Demande, 46 pp.
 CODEN: FRXXBL
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2835829	A1	20030815	FR 2002-1791	20020213
WO 2003068712	A2	20030821	WO 2003-FR464	20030213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: FR 2002-1791 A 20020213

AB The present invention relates to a method for preparation of a biochip which is
 activated for the covalent attachment of oligonucleotide or peptide probes
 on a solid support by a NHS-PEG-VS spacer. The invention also includes
 methods for detection of nucleic acids or peptides using biochips. The
 present invention also provides kits for detection, quant. or qual. anal.
 of nucleic acids or peptides in a sample, for purification of nucleic acids or
 peptides, for sequencing of nucleic acids, and for gene expression
 profiling or for the study and the detection of genetic polymorphisms for
 diagnosis of diseases.

IC ICM C07B051-00

ICS G01N033-543; C07K001-14; C12Q001-68
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 3, 14
IT **Amines**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(primary, deactivation of NHS on biochip using; methods for preparation of
DNA or protein microarrays)
IT **Amino group**
Sulphydryl group
(probe attached to biochip via; methods for preparation of DNA or
protein microarrays)
IT **Cyanine dyes**
(probe **conjugate**, **sulfonated** derivative; methods for
preparation of DNA or **protein** microarrays)
IT **Nanocrystals**
Nanoparticles
(probe **conjugate**; methods for preparation of DNA or
protein microarrays)
IT 1760-24-3, N-(2-Aminoethyl)-3-**amino**-propyltrimethoxysilane
4420-74-0, (3-Mercaptopropyl trimethoxysilane 13598-78-2, Aminosilane
14044-97-4, Mercaptosilane
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(biochip support activated with; methods for preparation of DNA or
protein microarrays)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:472604 CAPLUS
DOCUMENT NUMBER: 139:49507
TITLE: Synthesis and use of affinity probes directed toward
adenine nucleotide-binding proteins
INVENTOR(S): Campbell, David A.; Wash, Paul
PATENT ASSIGNEE(S): Activx Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003050248	A2	20030619	WO 2002-US39073	20021205
WO 2003050248	A3	20040122		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

US 2003134303	A1	20030717	US 2002-213359	20020805
PRIORITY APPLN. INFO.:			US 2001-339424P	P 20011211

US 2002-213359 A 20020805

AB The invention relates to compns. and methods for the synthesis and use of adenosine nucleotide-binding protein-directed affinity labels. Adenosine nucleotide-binding proteins may be labeled with probes comprising adenosine, or an analog thereof, functionalized at the 5' position with reactive group capable of reacting with an amino acid side chain functionality at an adenosine nucleotide binding site, and at the 2' or 3' position with a tag for sequestering and/or identifying the resulting conjugate. In particular, one such probe is 5'-fluorosulfonylbenzoylamido-2'-(3')-(2-TAMRA-amidoethylcarbamoyl)adenosine, shown to effectively label EGF receptor tyrosine kinase in A431 cells and insulin receptor kinase in boiled rat liver lysate. The probes may be used for determining the presence

or

amount of one or more adenosine nucleotide-binding proteins in a complex mixture, particularly a cellular mixture, for screening for drugs, and other purposes associated with the presence of the adenine nucleotide-binding protein(s) in a cell or changes in the presence, amount, activity, or relative concentration of the active adenosine nucleotide-binding protein.

IC ICM C12N

CC 9-15 (Biochemical Methods)

IT Functional groups

(acryl, in adenosine **conjugates** with fluorophores; synthesis and use of affinity probes directed toward adenine **nucleotide-binding proteins**)

IT Fluorescent substances

(adenosine **conjugates**; synthesis and use of affinity probes directed toward adenine **nucleotide-binding proteins**)

IT Functional groups

(chloroacetyl, in adenosine **conjugates** with fluorophores; synthesis and use of affinity probes directed toward adenine **nucleotide-binding proteins**)

IT Functional groups

(fluorosulfonyl, in adenosine **conjugates** with fluorophores; synthesis and use of affinity probes directed toward adenine **nucleotide-binding proteins**)

IT Functional groups

(vinylsulfonyl, in adenosine **conjugates** with fluorophores; synthesis and use of affinity probes directed toward adenine **nucleotide-binding proteins**)

IT 79-04-9, Chloroacetyl chloride 402-55-1, 4-Fluorosulfonylbenzoylchloride 530-62-1 814-68-6, Acryloyl chloride 14365-44-7 24424-99-5, Di-tert-butyl dicarbonate 51600-11-4 120718-52-7, TAMRA 146616-66-2, BODIPY-FL, SE 343934-41-8 519054-52-5, Rhodamine green carboxylic acid succinimidyl ester

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis and use of affinity probes directed toward adenine nucleotide-binding proteins)

L31 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:454606 CAPLUS

DOCUMENT NUMBER: 139:31760

TITLE: Methods and kits containing nanoparticle conjugated oligonucleotide probes for detection of nucleic acids using PCR

INVENTOR(S): Storhoff, James J.; Fritz, Brett M.; Herrmann, Mark

PATENT ASSIGNEE(S): Nanosphere, Inc., USA

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003048769	A1	20030612	WO 2002-US38069	20021127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003143604	A1	20030731	US 2002-306630	20021127
PRIORITY APPLN. INFO.: US 2001-334644P P 20011130				
AB	<p>The present invention relates to the use of nanoparticle detection probes to monitor amplification reactions, especially polymerase chain reactions ('PCR'). More specifically, the present invention involves the use of nanoparticles oligonucleotide conjugates treated with a protective agent such as bovine serum albumin in an homogeneous assay format in order to quant. and qual. detect a target polynucleotide. A detectable change (preferably a color change) is brought about as a result of the hybridization of the oligonucleotides on the nanoparticles to the nucleic acid. The invention also provides compns. and kits comprising particles. The invention further provides methods of synthesizing unique nanoparticle-oligonucleotide conjugates, the conjugates. Finally, the invention provides a method of separating a selected nucleic acid from other nucleic acids. The preparation of colloidal gold nanoparticles from HAuCl₄ is described. Particles show a color change upon aggregation. 3'-Thiol terminated oligonucleotides were immobilized on the surface of these particles. Oligonucleotide dependent aggregation and color changes were demonstrated and the hybridization conditions optimized.</p>			
IC	ICM G01N033-53 ICS G01N033-00; G01N021-65; G01V005-00; G01J003-30; C12Q001-68; C07H019-00; C07H021-00; C07H021-02; C07H021-04			
CC	3-1 (Biochemical Genetics)			
IT	Section cross-reference(s): 9 Thiols (organic), biological studies RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses) (acid or amine -terminated, as protective agents for nanoparticle conjugated oligonucleotide probes; methods and kits containing nanoparticle conjugated oligonucleotide probes for detection of nucleic acids using PCR)			
IT	Albumins, biological studies Antibodies Caseins, biological studies DNA Organic compounds, biological studies Polymers, biological studies Polyoxyalkylenes, biological studies Proteins RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses) (as protective agents for nanoparticle conjugated			

oligonucleotide probes; methods and kits containing nanoparticle
conjugated oligonucleotide probes for detection of
nucleic acids using PCR)

IT Peptides, biological studies

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)

(thiol-containing, as linking agent for probe; methods and kits
containing nanoparticle conjugated oligonucleotide probes for detection of
nucleic acids using PCR)

IT 60-23-1, Mercaptoethylamine 71310-21-9, 11-Mercaptoundecanoic acid

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)

(thiol-based linking agent; methods and kits containing
nanoparticle conjugated oligonucleotide probes for detection of nucleic
acids using PCR)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:335251 CAPLUS

DOCUMENT NUMBER: 138:334049

TITLE: Efficient synthesis of **protein-
oligonucleotide conjugates**

INVENTOR(S): Farooqui, Firdous; Reddy, Parameswara M.

PATENT ASSIGNEE(S): Beckman-Coulter, Inc., USA

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035830	A2	20030501	WO 2002-US32317	20021011
W: AU, CA, CN, DE, GB, JP				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
US 2003092901	A1	20030515	US 2001-32592	20011024

PRIORITY APPLN. INFO.: US 2001-32592 A 20011024

AB The present invention relates to an improved method for forming a
protein-oligonucleotide conjugate. The method is particularly amenable
for forming antibody-oligonucleotide conjugates. The invention further
concerns the conjugate mols. produced using such improved methods.

IC ICM C12N

CC 9-14 (Biochemical Methods)

ST synthesis **protein oligonucleotide conjugate**

IT Antibodies

Oligonucleotides

Proteins

RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST
(Analytical study); PREP (Preparation)

(conjugates; efficient synthesis of **protein-
oligonucleotide conjugates**)

IT **Conjugation** (molecular association)

Immunoassay

Nucleic acid hybridization

(efficient synthesis of **protein-oligonucleotide
conjugates**)

IT Avidins

Biliproteins

Enzymes, analysis

Immunoglobulins

RL: ARU (Analytical role, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process)

(efficient synthesis of **protein-oligonucleotide conjugates**)

IT 4781-83-3, Traut's reagent

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)

(efficient synthesis of **protein-oligonucleotide conjugates**)

IT 9001-78-9, Alkaline phosphatase 9002-13-5, Urease 9013-20-1, Streptavidin 9031-11-2, β -Galactosidase

RL: ARU (Analytical role, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process)

(efficient synthesis of **protein-oligonucleotide conjugates**)

IT 103708-09-4, Sulfo-SMCC

RL: RCT (Reactant); RACT (Reactant or reagent)

(efficient synthesis of **protein-oligonucleotide conjugates**)

IT 9003-99-0, Peroxidase

RL: ARU (Analytical role, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process)

(horseradish; efficient synthesis of **protein-oligonucleotide conjugates**)

L31 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:173820 CAPLUS

DOCUMENT NUMBER: 138:182042

TITLE: Methods for haplotyping analysis by detection of single nucleotide polymorphisms

INVENTOR(S): Fenger, Mogens; Bentzen, Joan

PATENT ASSIGNEE(S): Hvidovre Hospital, Den.

SOURCE: PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018835	A2	20030306	WO 2002-DK552	20020822
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: DK 2001-1252 A 20010823

AB The present invention describes a method and kits for determining the genetic

haplotype (linkage phase) of a part of an individual genotype, by determining the presence or absence of two or more specific nucleotide polymorphisms on one of a pair of homologous chromosomes. Amplification of nucleic acids may be performed by PCR, Ligase Chain Reaction, Nucleic-Acid Sequence-Based Amplification, strand displacement amplification, rolling circle amplification, T7-polymerase amplification.

IC ICM C12Q001-68

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 9

IT **Proteins**

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(A, **oligonucleotide probe conjugate**; methods for haplotyping anal. by detection of single **nucleotide** polymorphisms)

IT Immunoglobulins

Proteins

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(G, **oligonucleotide probe conjugate**; methods for haplotyping anal. by detection of single **nucleotide** polymorphisms)

IT **Sulfhydryl group**

(nucleic acid conjugate; methods for haplotyping anal. by detection of single nucleotide polymorphisms)

IT **Amines, biological studies**

Phosphates, biological studies

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primary, nucleic acid conjugate; methods for haplotyping anal. by detection of single **nucleotide** polymorphisms)

L31 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:160521 CAPLUS

DOCUMENT NUMBER: 138:216548

TITLE: DNA and protein sequences of Rhodococcus erythropolis cystathionine β -synthase sequence homolog and the uses of the protein for repression of the expression of the genes for desulfurization

INVENTOR(S): Kurane, Ryuichiro; Tanaka, Yasuhiro; Marubashi, Kenji

PATENT ASSIGNEE(S): National Institute of Advanced Industrial Science and Technology, Japan; Kokusai Sekiyu Koryu Center

SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003061669	A2	20030304	JP 2001-254269	20010824

PRIORITY APPLN. INFO.: JP 2001-254269 20010824

AB The invention provides DNA and protein sequences for a gene from Rhodococcus erythropolis sharing sequence homol. with Streptomyces venezuela cystathionine β -synthase. The gene was identified by randomly knocking out the genes associated with desulfurization in thiophene degradable microorganism. The gene can be used for producing of **sulfate** ion independent desulfurization microorganism.

IC ICM C12N015-09

ICS C12N001-20; C12N001-21; C12R001-01; C12R001-32; C12R001-125;
C12R001-10; C12R001-06; C12R001-19; C12R001-40; C12R001-385;
C12R001-39

CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 10

IT 91-20-3D, Naphthalene, thiophene **conjugates** 95-15-8,
Benzothiophene 110-02-1D, Thiophene, naphthyl derivs. 110-82-7D,
Cyclohexane, dibenzothiophene **conjugates** 132-65-0, Dibenzo
thiophene 132-65-0D, Dibenzothiophene, cyclohexyl derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**DNA** and **protein** sequences of Rhodococcus
erythropolis cystathionine β -synthase sequence homolog and the
uses of the **protein** for repression of the expression of the
genes for desulfurization)

IT 500686-67-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(**amino** acid sequence; **DNA** and protein sequences of
Rhodococcus erythropolis cystathionine β -synthase sequence homolog
and the uses of the protein for repression of the expression of the
genes for desulfurization)

L31 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:937303 CAPLUS

DOCUMENT NUMBER: 138:20443

TITLE: Endocrine disruptor screening using DNA chips of
endocrine disruptor-responsive genes

INVENTOR(S): Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi;
Tsujiimoto, Yoshimasa; Takashima, Ryokichi; Enoki,
Yuki; Kato, Ikunoshin

PATENT ASSIGNEE(S): Takara Bio Inc., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 386 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002355079	A2	20021210	JP 2002-69354	20020313
PRIORITY APPLN. INFO.:				
			JP 2001-73183	A 20010314
			JP 2001-74993	A 20010315
			JP 2001-102519	A 20010330

AB A method and kit for detecting endocrine-disrupting chems. using DNA
microarrays are claimed. The method comprises preparing a nucleic acid
sample containing mRNAs or cDNAs originating in cells, tissues, or organisms
which have been brought into contact with a sample containing the endocrine
disruptor. The nucleic acid sample is hybridized with DNA microarrays
having genes affected by the endocrine disruptor or DNA fragments
originating in these genes have been fixed. The results obtained are then
compared with the results obtained with the control sample to select the
gene affected by the endocrine disruptor. Genes whose expression is
altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate,
dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl
phthalate, diethylstilbestrol (DES), and 17- β estradiol (E2), were
found in mice by DNA chip anal.

IC ICM C12N015-09

ICS C12N015-09; C12Q001-02; C12Q001-68; G01N033-53; G01N037-00

CC 3-1 (Biochemical Genetics)

- Section cross-reference(s): 2, 4, 5, 9, 13
- IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E74-like **factor 1** (ets domain transcription factor);
endocrine disruptor screening using DNA chips of endocrine
disruptor-responsive genes)
- IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HMG-box containing protein 1; endocrine disruptor screening using
DNA chips of endocrine disruptor-responsive genes)
- IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HSPC015; endocrine disruptor screening using **DNA**
chips of endocrine disruptor-responsive genes)
- IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**KIAA0033**; endocrine disruptor screening using DNA chips of
endocrine disruptor-responsive genes)
- IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PNO099 son3 **protein**; **endocrine** disruptor
screening using **DNA** chips of endocrine disruptor-
responsive genes)
- IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PTH-responsive osteosarcoma **B1 protein**;
endocrine disruptor screening using **DNA** chips of
endocrine disruptor-responsive genes)
- IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chondroitin **sulfate**-containing; endocrine disruptor screening
using DNA chips of endocrine disruptor-responsive genes)
- IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(muscle-blind, sequence **homolog**; endocrine disruptor
screening using DNA chips of endocrine disruptor-responsive genes)
- IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(myelocytomatosis oncogene; endocrine disruptor screening using DNA
chips of endocrine disruptor-responsive genes)
- IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(myeloid differentiation primary **response** gene (88);
endocrine disruptor screening using DNA chips of endocrine
disruptor-responsive genes)
- IT Nicotinic receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nicotinic cholinergic **receptor**, β **polypeptide**
1 (muscle); endocrine disruptor screening using DNA chips of endocrine
disruptor-responsive genes)
- IT **Transport proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**nucleoside transporter**, equilibrative
nitrobenzyl-thioinosine sensitive nucleoside transporter
ENT1; endocrine disruptor screening using DNA chips of
endocrine disruptor-responsive genes)
- IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(protein tyrosine phosphatase receptor type f polypeptide (PTPRF)
interacting protein (liprin) $\alpha 1$; endocrine disruptor screening

- using DNA chips of endocrine disruptor-responsive genes)
- IT **Proteins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (retinol binding protein, CRBP (cellular **retinol** binding protein), cellular retinol binding protein 2; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)
- IT **Cytokines**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (small inducible **cytokine** A27, A9, A5; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)
- IT **Proteins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (synuclein γ ; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)
- IT 37278-34-5, Heparitin N-deacetylase/N-**sulfotransferase**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (-N-deacetylase; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)
- IT 9023-09-0, **Sulfotransferase**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (2B member 1; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)
- IT 9023-05-6, **Sulfurtransferase**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (3 MERCA-pitopyruvate **sulfurtransferase**; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)
- IT 73361-25-8, Heparitin N-deacetylase/N-**sulfotransferase**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (N-**sulfotransferase**; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)
- IT 110463-31-5, **Amine N-sulfotransferase**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (**amine N-sulfotransferase**; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)
- IT 1393-25-5, Secretin 9000-94-6, Antithrombin-III 9001-05-2, Catalase
 9001-16-5, Cytochrome c oxidase 9001-40-5, Glucose-6 phosphate dehydrogenase 9001-42-7, α -Glucosidase 9001-45-0, Glucuronidase β 9001-48-3, Glutathione reductase 9001-50-7, Glyceraldehyde-3-phosphate dehydrogenase 9001-61-0, Cytosolic aminopeptidase 9001-63-2, Lysozyme 9001-64-3, Malate dehydrogenase 9001-91-6, Plasminogen 9002-03-3, Dihydrofolate reductase 9002-62-4, Prolactin, biological studies 9004-02-8, Lipoprotein lipase 9012-37-7, Aminoacylase-1 9012-93-5, Ferrochelataase 9013-10-9, Glucosamine-6-phosphate isomerase 9013-93-8, Phospholipase 9014-18-0, Nicotinamide nucleotide transhydrogenase 9023-44-3, Tryptophanyl-tRNA synthetase 9023-48-7, Seryl-tRNA synthetase 9023-56-7, CTP synthase 9023-58-9, Argininosuccinate synthetase 9023-69-2, Asparagine synthetase 9023-88-5 9023-90-9, Methylmalonyl-CoA mutase 9024-20-8, Ribulose phosphate 3 epimerase 9024-60-6, Ornithine decarboxylase 9024-70-8, Uroporphyrinogen decarboxylase 9025-15-4, Biotinidase 9025-73-4, Phosphoserine phosphatase 9026-00-0, Lysosomal acid lipase 9026-23-7, Carbamoyl-phosphate synthase 9026-24-8, Thiamin pyrophosphokinase 9026-30-6, Poly (A) polymerase 9026-67-9, Choline kinase 9027-13-8, Enoyl-CoA hydratase 9027-32-1, Aspartyl-tRNA synthetase 9027-44-5, Hydroxymethylglutaryl-CoA synthase 9027-67-2, Terminal deoxynucleotidyl transferase 9027-80-9, Adenine phosphoribosyl transferase 9027-81-0, Adenylosuccinate Lyase 9028-21-1, Sorbitol dehydrogenase 9028-40-4, 3-Hydroxyacyl-CoA dehydrogenase 9028-61-9, Estradiol 17 β -dehydrogenase 9029-17-8, Pyrroline-5-carboxylate reductase

9029-38-3, **Sulfite** oxidase 9030-22-2, Uridine phosphorylase
 9030-23-3, Thymidine phosphorylase 9030-24-4, Uracil
 phosphoribosyltransferase 9030-38-0 9030-53-9, Galactokinase
 9030-83-5, 3-Hydroxy-3-methylglutaryl-CoA lyase 9031-19-0, Saccharopine
 dehydrogenase 9031-37-2, Ceruloplasmin 9031-71-4, Alanyl-tRNA
 synthetase 9031-82-7, Amidophosphoribosyltransferase 9031-86-1,
 Aspartoacylase 9032-03-5, Phosphoribosylaminoimidazolecarboxamide
 formyltransferase 9032-25-1, NADH cytochrome B5 reductase 9032-59-1,
 Fumarylacetoacetate hydrolase 9032-71-7, 2,3-Oxidosqualene-lanosterol
 cyclase 9032-73-9, Neuropathy target esterase 9032-88-6, Fumarate
 hydratase 9033-27-6, Isopentenyl-diphosphate δ isomerase
 9035-39-6, Cytochrome b5 9035-42-1, Cytochrome c1 9037-62-1,
 Glycyl-tRNA synthetase 9037-65-4, α -L-Fucosidase 9040-59-9,
 Phosphodiesterase 1 9042-64-2, DOPA decarboxylase 9045-77-6, Fatty
 acid synthase 9047-22-7, Cathepsin B 9054-54-0, Transacylase
 9054-84-6, Xanthine dehydrogenase 9059-11-4, **Amine** oxidase
 9059-48-7, Sepiapterin reductase 9067-83-8, Phosphatidate
 cytidyltransferase 9068-16-0, Poly(ADP ribose) glycohydrolase
 9068-41-1, Carnitine palmitoyltransferase 9074-91-3, Hydroxymethylbilane
 synthase 9075-29-0, 3 Phosphoglycerate dehydrogenase 9075-78-9,
 Ethanolamine kinase 9075-81-4, β -Galactoside α -2,6-
 sialyltransferase 9076-57-7, Histone deacetylase 9076-84-0,
 Coproporphyrinogen oxidase 12651-28-4, Transcobalamin 2 37184-63-7,
 Myoinositol 1-monophosphatase 37205-49-5, Methylmalonate-semialdehyde
 dehydrogenase 37211-69-1, 2,3-Bisphosphoglycerate mutase 37237-43-7,
 Galactosyltransferase β -1,4-GalT V 37255-37-1, E.C. 1.3.3.2
 37255-38-2, Glutaryl-CoA dehydrogenase 37259-54-4, DTDP-glucose
 4,6-dehydratase 37274-61-6, Isovaleryl-CoA dehydrogenase 37277-82-0,
 Spermidine synthase 37341-57-4, Succinate:CoA ligase 39471-28-8,
 Deoxyguanosine kinase 51110-01-1, Somatostatin 52660-18-1, Casein
 kinase 1 55354-43-3, Arylsulfatase B 59088-23-2, Dihydroorotate
 dehydrogenase 59298-90-7, UDP-galactose:glucosylceramide
 β 1,4-galactosyltransferase 60320-99-2, N-Acetylglucosamine-6-
sulfatase 65997-74-2, Cathepsin F 67339-00-8,
 α 2,8-Sialyltransferase 67763-97-7, Insulin-like growth factor 2
 79079-11-1, Calpastatin 80295-40-5, Complement C2 80295-48-3,
 Complement C4 80295-62-1, Complement factor B 80295-65-4, Complement
 factor H 81181-72-8, γ -Glutamyl carboxylase 81611-75-8,
 Fructose-2,6-bisphosphatase 82062-90-6, NAD-dependent
 methylenetetrahydrofolate dehydrogenase 82391-38-6, Branched chain keto
 acid dehydrogenase kinase 82707-54-8, Neprilysin 83268-44-4
 86480-67-3, Ubiquitin carboxyl-terminal hydrolase 87683-70-3,
 Pterin-4 α -carbinolamine dehydratase 90698-32-1, Leukotriene C4
 synthase 101149-94-4, Tripeptidyl peptidase II 102577-19-5, Neuromedin
 B 109136-49-4, Ubiquitin-specific protease 122320-05-2, Secretory
 leukocyte protease inhibitor 124861-55-8 137632-08-7, Mitogen
 activated protein kinase 1 141349-86-2, Cyclin-dependent kinase 2
 141467-21-2, Calcium/calmodulin-dependent protein kinase I 142243-03-6,
 Plasminogen activator inhibitor type II 142539-77-3, Mast cell protease
 5 142805-56-9, DNA topoisomerase II 143180-75-0, DNA topoisomerase I
 144114-16-9, Focal adhesion kinase 144697-17-6, c-Src tyrosine kinase
 145809-21-8, Tissue inhibitor of metalloproteinase 3 146480-35-5, Matrix
 metalloproteinase 2 146480-49-1, MMCP-6 protease 146838-30-4,
 Mitogen-activated protein kinase-activated protein kinase 2 147014-97-9,
 Cyclin dependent kinase 4 149316-81-4, 2-Hydroxyphytanoyl-CoA lyase
 149371-24-4, Neurolysin 150605-50-8, Neuronal tyrosine/threonine
 phosphatase 1 152478-57-4, Janus kinase 2 153190-47-7, Gene PTK2
 tyrosine kinase 165245-94-3, NIMA-related kinase 2 165245-99-8,
 Polo-like kinase 167397-96-8, Interleukin-1 receptor-associated kinase
 169277-44-5, Sphingosine-1-phosphate phosphatase 169592-62-5,

Cyclin-dependent kinase 10 170780-57-1, LIM kinase 172306-41-1,
 Protein kinase PCTAIRE-1 172399-47-2, BOMAPIN 173585-04-1,
 Integrin-linked kinase 176023-64-6, Mitogen-activated protein kinase 12
 178037-70-2, Serum and glucocorticoid regulated protein kinase
 180189-96-2, Caspase 9 182372-15-2, Caspase 6 184049-62-5, Gene DUSP6
 MAP kinase phosphatase 187247-72-9, Endonuclease G 188417-84-7,
 Vascular endothelial growth factor C 191359-13-4, MAP kinase-interacting
 kinase 1 192230-91-4, Mitogen-activated protein kinase kinase 4
 194739-73-6, Mitogen-activated protein kinase kinase 6 196717-99-4,
 Prenylcysteine lyase 206566-35-0, Molybdopterin synthase
sulfurylase 212625-17-7, SPAK protein kinase 214210-47-6,
 Neuropilin 1 216503-96-7, Caspase 11 223610-95-5, Matrix
 metalloproteinase MMP-23 230951-53-8, Caspase 12 252852-50-9, SUMO-1
 conjugate proteinase 252901-98-7, Tousled-like kinase 1 258336-77-5,
 UNC51.2 serine/threonine kinase 288307-53-9, Inositol
 1,3,4-trisphosphate 5/6 kinase 292850-69-2, Nardilysin 306298-47-5,
 MAP kinase phosphatase-1 321976-25-4, Sialyltransferase 324751-96-4,
 Stanniocalcin 2 324752-01-4, Stanniocalcin 1 327046-95-7, Mitogen
 activated protein kinase kinase 5 335135-28-9, Cytochrome P450 2D10
 338969-69-0, Cytochrome P450 2F2 353498-78-9, Mitogen activated protein
 kinase 6 362516-16-3, Conserved helix-loop-helix ubiquitous kinase
 374936-45-5, Cytochrome P450 2C40 409105-92-6, Microtubule-associated
 testis-specific serine/threonine protein kinase 440356-82-1, Cytochrome
 P450 7B1 443906-18-1, Receptor protein tyrosine phosphatase K
 464896-43-3, Transmembrane serine proteinase 475489-73-7,
 Calcium/calmodulin-dependent protein kinase II 478187-31-4, P 450 2J6
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (endocrine disruptor screening using DNA chips of endocrine
 disruptor-responsive genes)

L31 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:734843 CAPLUS

DOCUMENT NUMBER: 138:68558

TITLE: Site-specific DNA cleavage of synthetic NarL sites by
 an engineered Escherichia coli NarL
 protein-1,10-phenanthroline cleaving agent

AUTHOR(S): Xiao, Gaoping; Cole, Daniel L.; Gunsalus, Robert P.;
 Sigman, David S.; Chen, Chi-Hong B.

CORPORATE SOURCE: Department of Microbiology, Immunology, University of
 California, Los Angeles, CA, 90095-1489, USA

SOURCE: Protein Science (2002), 11(10), 2427-2436

CODEN: PRCIEI; ISSN: 0961-8368

PUBLISHER: Cold Spring Harbor Laboratory Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The NarL response regulatory protein of Escherichia coli has been
 engineered by covalent modification with 1,10-phenanthroline (OP) to
 create a set of site-specific DNA-cleaving agents. This was accomplished
 by introducing single cysteine amino acid replacements at
 selected locations within the C-terminal DNA-binding domain in
 or nearby the helix 8 to helix 9 region of the NarL protein using
 site-directed mutagenesis. Of 18 modified NarL-OP proteins made, 13
 retained the ability to bind DNA as evidenced by gel mobility assays,
 whereas 10 of the 1,10-phenanthroline-modified proteins also exhibited
 specific cleavage activity for a synthetic NarL recognition sequence.
 These DNA-cleaving agents were divided into two groups based on the
 location of the cleavage sites. The first class set cleaved the DNA
 nearby the center of a synthetic 7-2-7 sequence composed of two NarL
 heptamer sites separated by a 2-bp spacer element. The second class cut the
 DNA at the periphery of the 7-2-7 sequence. The cleavage data are

consistent with the ability of two NarL monomers to recognize and bind to the DNA in a head-to-head orientation. A second set of DNA-cleaving agents was constructed using the C-terminal domain of NarL called NarLC. Similar cleavage patterns were observed whether full-length NarL or NarLC was used. The availability of 1,10-phenanthroline-modified NarL and NarLC proteins opens up the possibility to explore the position, orientation, and number of NarL recognition sites at E. coli promoters predicted to contain multiple and complex arrangements of NarL-binding sites.

- CC 6-3 (General Biochemistry)
Section cross-reference(s): 3, 9
- IT 52-90-4D, L-Cysteine, **conjugates** with orthophenanthroline
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(residues 162, 174, 181, 201, 204 or 211 of NarL; site-specific
DNA cleavage of synthetic NarL sites by an engineered
Escherichia coli NarL **protein**-1,10-phenanthroline cleaving
agent)
- IT 111047-29-1D, **conjugates** with NarL **proteins**
182685-66-1D, **conjugates** with NarL **proteins**
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(site-specific **DNA** cleavage of synthetic NarL sites by an
engineered Escherichia coli NarL **protein**-1,10-phenanthroline
cleaving agent)
- IT 107-96-0, 3-Mercaptopropionic acid 7722-84-1, Hydrogen peroxide,
reactions 7758-98-7, Copper **sulfate**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(site-specific **DNA** cleavage of synthetic NarL sites by an engineered
Escherichia coli NarL protein-1,10-phenanthroline cleaving agent)
- REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:367208 CAPLUS

DOCUMENT NUMBER: 136:366115

TITLE: Ligand-aminodextran-marker **conjugates** and
uses thereof

INVENTOR(S): Siiman, Olavi; Burshteyn, Alexander; Mylvaganam,
Ravindra; Raynor, Robert; Roth, Patricia; Smith,
Cecilia; Wilkinson, Julie

PATENT ASSIGNEE(S): Coulter International Corp., USA

SOURCE: U.S., 58 pp., Cont.-in-part of U.S. 5,994,089.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6387622	B1	20020514	US 1999-403919	19991027
US 5891741	A	19990406	US 1997-857941	19970516
US 5994089	A	19991130	US 1997-976031	19971121
WO 9852040	A1	19981119	WO 1998-US9774	19980514
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1997-857941 A2 19970516

US 1997-976031 A2 19971121

WO 1998-US9774 W 19980514

AB Ligand-aminodextran-(phycobiliprotein or tandem dye) **conjugates**

useful for detection of a desired target biol. material by providing an enhanced fluorescent signal are described. Also described is a method for a single-measurement quantification of multiple populations of cells based upon the labeling of different pairs of cell populations, each pair containing mutually exclusive cell receptors which are expressed at substantially similar receptor densities with labeled ligands for each receptor. One cell population is labeled with a ligand capable of binding to a first cell surface receptor which ligand is directly **conjugated** to a fluorescent phycobiliprotein or tandem dye; and a second cell population is labeled with a ligand capable of binding to a second cell surface receptor, which ligand is cross-linked to an aminodextran which is **conjugated** to a fluorescent phycobiliprotein or tandem dye. Monoclonal antibody-phycoerythrin **conjugates** and monoclonal antibody-aminodextran-phycoerythrin **conjugates** were prepared and used in flow cytometric anal. of whole blood.

IC ICM G01N033-68

NCL 435006000

CC 9-4 (Biochemical Methods)

Section cross-reference(s): 15

ST ligand aminodextran marker **conjugate** flow cytometry; fluorescent phycobiliprotein ligand aminodextran flow cytometry; monoclonal antibody aminodextran phycoerythrin **conjugate** blood analysis

IT Cyanine dyes

(5.1, **conjugates** with phycoerythrin and with ligand; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Allophycocyanins

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(B, **conjugates** with ligands; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Immunoglobulins

RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(G1, monoclonal; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Immunoglobulins

RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(M; monoclonal; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Histocompatibility antigens

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(MHC (major histocompatibility complex), complexes with peptide and streptavidin or avidin, as ligand; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Peptides, preparation

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(MHC complexes and complexes with streptavidin or avidin, as ligand; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Phycoerythrins

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(R-phycoerythrins, **conjugates** with ligands; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Biological materials

(anal. of; ligand-aminodextran-marker **conjugates** and uses thereof)

IT CD19 (antigen)

CD3 (antigen)

CD45RO (antigen)

CD56 (antigen)

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody to; ligand-aminodextran-marker **conjugates** and uses
thereof)

IT **Proteins**

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(blue fluorescent, as label; ligand-aminodextran-marker
conjugates and uses thereof)

IT **Avidins**

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
(Analytical study); PREP (Preparation); USES (Uses)
(complexes with MHC-peptide, as ligand; ligand-aminodextran-marker
conjugates and uses thereof)

IT **Ligands**

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**conjugated**; ligand-aminodextran-marker **conjugates**
and uses thereof)

IT **Allophycocyanins**

Biliproteins

Phycocyanins

Phycoerythrins

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**conjugates** with ligands; ligand-aminodextran-marker
conjugates and uses thereof)

IT **Oligonucleotides**

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**conjugates**; ligand-aminodextran-marker **conjugates**
and uses thereof)

IT **Antibodies**

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
(Analytical study); PREP (Preparation); USES (Uses)
(**conjugates**; ligand-aminodextran-marker **conjugates**
and uses thereof)

IT **Cytometry**

(flow; ligand-aminodextran-marker **conjugates** and uses
thereof)

IT **Immunoglobulins**

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fragments, **conjugates**; ligand-aminodextran-marker
conjugates and uses thereof)

IT **Proteins**

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(green fluorescent, as label; ligand-aminodextran-marker
conjugates and uses thereof)

IT **Interleukin receptors**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interleukin 12, β chain, monoclonal antibody to human;
ligand-aminodextran-marker **conjugates** and uses thereof)

IT **Interleukin 12**

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical
study); BIOL (Biological study)
(ligand as antibody to; ligand-aminodextran-marker **conjugates**
and uses thereof)

IT **Blood analysis**

Fluorescence

Human

Leukocyte

T cell (lymphocyte)

(ligand-aminodextran-marker **conjugates** and uses thereof)

- IT Nucleic acids
RL: ANT (Analyte); ANST (Analytical study)
(ligand-aminodextran-marker **conjugates** and uses thereof)
- IT Receptors
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(ligands binding to; ligand-aminodextran-marker **conjugates** and uses thereof)
- IT CD8 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoclonal antibody to; ligand-aminodextran-marker **conjugates** and uses thereof)
- IT Antibodies
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(monoclonal, **conjugates**; ligand-aminodextran-marker **conjugates** and uses thereof)
- IT Antibodies
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(monoclonal; ligand-aminodextran-marker **conjugates** and uses thereof)
- IT Lymphocyte
(natural killer cell, monoclonal antibody to human; ligand-aminodextran-marker **conjugates** and uses thereof)
- IT Molecular weight
(of antibody-aminodextran-phycoobiliprotein **conjugates**; ligand-aminodextran-marker **conjugates** and uses thereof)
- IT Dyes
(phycoobiliprotein-containing tandem, **conjugates** with ligand; ligand-aminodextran-marker **conjugates** and uses thereof)
- IT Cell
(single-measurement quantification of multiple populations of; ligand-aminodextran-marker **conjugates** and uses thereof)
- IT 9004-54-0, Dextran, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(T-2M; ligand-aminodextran-marker **conjugates** and uses thereof)
- IT 109-76-2, 1,3-Diaminopropane
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(aminodextran substituted with; ligand-aminodextran-marker **conjugates** and uses thereof)
- IT 9013-20-1DP, Streptavidin, complexes with MHC-peptide
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(as ligand; ligand-aminodextran-marker **conjugates** and uses thereof)
- IT 27072-45-3D, FITC, **conjugates** with antibody to CD45RO
82354-19-6D, Texas Red, **conjugates** with phycoerythrin and with ligand
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(ligand-aminodextran-marker **conjugates** and uses thereof)
- IT 37293-51-9DP, Aminodextran, **conjugates** with phycoobiliprotein or tandem dye and **crosslinked** with ligand 88475-75-6DP, ECD, **conjugates** with aminodextran and ligand 146368-14-1DP, Cy5, **conjugates** with allophycocyanin and with ligand 169799-14-8DP, Cy7, **conjugates** with phycoerythrin or allophycocyanin and with ligand
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST

(Analytical study); PREP (Preparation); USES (Uses)
 (ligand-aminodextran-marker **conjugates** and uses thereof)
 IT 37293-51-9, Aminodextran
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (ligand-aminodextran-marker **conjugates** and uses thereof)
 IT 6539-14-6, 2-Iminothiolane
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction with R-phycoerythrin or monoclonal antibody;
 ligand-aminodextran-marker **conjugates** and uses thereof)
 IT 103708-09-4, **Sulfo-SMCC**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction with monoclonal antibodies or aminodextran;
 ligand-aminodextran-marker **conjugates** and uses thereof)
 REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2001:265431 CAPLUS
 DOCUMENT NUMBER: 134:291071
 TITLE: High affinity RNase H-recruiting oligonucleotides
 containing bicyclic nucleoside analogs
 INVENTOR(S): Wahlestedt, Claes; Jakobsen, Mogens Havsteen
 PATENT ASSIGNEE(S): Exiqon A/S, Den.
 SOURCE: PCT Int. Appl., 16 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001025248	A2	20010412	WO 2000-DK550	20001003
WO 2001025248	A3	20010830		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1224280	A2	20020724	EP 2000-962273	20001003
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003511016	T2	20030325	JP 2001-528192	20001003
PRIORITY APPLN. INFO.:				
			DK 1999-1422	A 19991004
			US 1999-157724P	P 19991005
			WO 2000-DK550	W 20001003
AB The present invention relates to the field of bicyclic DNA analogs, e.g., LNA and LNA modifications, which are useful for designing oligomers that form high affinity duplexes with complementary RNA wherein said duplexes are substrates for RNase H. The oligonucleotides may be partially or fully composed of LNA analogs with very high affinity and ability to recruit RNase H. The implications are that oxy-LNA by itself may be used to construct novel antisense mols. with enhanced biol. activity. Alternatively, oxy-LNA may be used in combination with non-oxy-LNA, such as standard DNA, RNA or other analogs, e.g. thio-LNA or				

amino-LNA, to create high affinity, RNase H recruiting anti-sense compds. without the need to adhere to any fixed design.

IC ICM C07H021-00

CC 3-1 (Biochemical Genetics)

IT Antibodies

Enzymes, biological studies

Haptens

Peptides, biological studies

Polysaccharides, biological studies

Proteins, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(conjugates with locked nucleic acids; high affinity RNase H-recruiting **oligonucleotides** containing bicyclic nucleoside analogs)

L31 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:457085 CAPLUS

DOCUMENT NUMBER: 133:85091

TITLE: Targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors

INVENTOR(S): Boucher, Richard C., Jr.; Pickles, Raymond J.; Rideout, Janet L.; Pendergast, William; Yerxa, Benjamin R.; Douglass, James G., III

PATENT ASSIGNEE(S): The University of North Carolina At Chapel Hill, USA

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039145	A1	20000706	WO 1999-US30658	19991222
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1140967	A1	20011010	EP 1999-966577	19991222
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

PRIORITY APPLN. INFO.: US 1998-219672 A 19981223
US 1998-219698 A 19981223
WO 1999-US30658 W 19991222

OTHER SOURCE(S): MARPAT 133:85091

AB A method of delivering foreign nucleic acid (e.g., a gene) into a cell by attaching a virus containing the nucleic acid to a G protein coupled receptor (i.e., a seven transmembrane receptor such as the P2Y2 receptor) that is internalized upon ligand binding. The virus may be attached to the receptor by means of a bridging antibody, or by binding an antibody specific for the receptor with an antibody specific for the virus, wherein the antibody that specifically binds with the receptor and the antibody that specifically binds to the virus are cross-linked.

Alternatively, the virus may express a peptide that specifically binds to

the receptor. The receptor may be induced to internalize by means of the addition of a ligand known to trigger internalization of the receptor into the cell. Purinoceptors, specifically the P2Y2 receptor, were identified on the surface of the apical surface of the airway epithelium. Cells presenting the P2Y2 receptor containing a hemagglutinin epitope were incubated with adenovirus carrying a lacZ reporter gene and labeled with a bispecific antibody to the epitope and the knob protein of adenovirus. The virus was rapidly internalized upon exposing the cells to ATP γ S.

- IC ICM C07H021-00
ICS C07H021-02; A61K009-12; A61K031-70
- CC 3-1 (Biochemical Genetics)
- ST G **protein** coupled receptor vector internalization; endocytosis
transforming DNA G **protein** coupled receptor
- IT Bradykinin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(B2; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Purinoceptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(P2U; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Adeno-associated virus
Herpesviridae
Human adenovirus
Lentivirus
Murine leukemia virus
Retroviral vectors
(as gene transfer vector; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(conjugates, in binding of virus vectors to G **protein** coupled receptors; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Oligonucleotides
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(dinucleotides, in stimulation of uptake of viral vectors bound to G **protein**-couple receptors; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Respiratory tract
(epithelium, transformation of cells of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Hemagglutinins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(epitope of, in targetting of viral gene transfer vectors; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Cystic fibrosis
(gene therapy of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

- IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in binding of virus vectors to G **protein**-coupled receptors; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Catecholamines, biological studies
Nucleosides, biological studies
Nucleotides, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(in stimulation of uptake of viral vectors bound to G **protein** -couple receptors; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Biological transport
(internalization, receptor-mediated; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Endocytosis
(receptor-mediated; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Gene therapy
(targeted gene delivery in; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Transformation, genetic
Virus vectors
(targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT G **protein**-coupled receptors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
($\alpha\beta 3$, in internalization of adenovirus; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
($\alpha\beta 5$, in internalization of adenovirus; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT Adrenoceptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
($\beta 2$; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
- IT 58-82-2P, Bradykinin 80295-54-1P, Complement C5a
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(in stimulation of uptake of viral vectors bound to G **protein** -couple receptors; targeted gene transfer and internalization of virus

vectors using G **protein** coupled receptors)

IT 280549-85-1P
 RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation and reactions of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT 280549-82-8P 280549-83-9P 280549-84-0P 280549-87-3P,
 2-Bromo-4'-[(6-bromohexanoyl)amino]acetophenone 280549-89-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reactions of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT 280549-76-0P 280549-78-2P 280549-80-6P 280549-91-9P 280549-92-0P
 280549-94-2P
 RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation and uses of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT 58-97-9, Uridine 5'-monophosphate, reactions 99-92-3,
 4'-Aminoacetophenone 530-62-1 22809-37-6, 6-Bromohexanoyl chloride 72040-63-2, Succinimidyl-6-(biotinamido) hexanoate 93285-75-7,
 N-Iodoacetyl-N'-biotinylnhexylenediamine 109276-34-8 280549-77-1
 280549-79-3 280549-81-7 280549-86-2 280549-88-4,
 4'-[(6-Bromohexanoyl)amino]acetophenone 280549-90-8 280549-93-1
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactions of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT 60-23-1, Mercaptoethylamine 92921-25-0, Sulfo-MBS 185332-92-7, Sulfo-GMBS
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:254039 CAPLUS

DOCUMENT NUMBER: 132:289590

TITLE: Peptide-enhanced cationic lipid transfections

INVENTOR(S): Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen; Jessee, Joel A.; Schifferli, Kevin P.; Gebeyehu, Gulilat

PATENT ASSIGNEE(S): Life Technologies, Inc., USA

SOURCE: U.S., 103 pp., Cont.-in-part of U.S. 5,736,392.
 CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6051429	A	20000418	US 1997-818200	19970314
US 5736392	A	19980407	US 1996-658130	19960604
WO 9840502	A1	19980917	WO 1998-US5232	19980316

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
 UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
 FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
 GA, GN, ML, MR, NE, SN, TD, TG

AU 9865622 A1 19980929 AU 1998-65622 19980316

EP 1007699 A1 20000614 EP 1998-911737 19980316

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI

JP 2001517939 T2 20011009 JP 1998-539899 19980316

US 6376248 B1 20020423 US 1998-39780 19980316

US 2003144230 A1 20030731 US 2002-200879 20020723

PRIORITY APPLN. INFO.:

US 1995-477354 B2 19950607

US 1996-658130 A2 19960604

US 1997-818200 A 19970314

US 1998-39780 A1 19980316

WO 1998-US5232 W 19980316

US 2001-911569 A1 20010723

AB The present invention provides comps. useful for transfecting eukaryotic cells comprising nucleic acid complexes with peptides, wherein the peptide is optionally covalently coupled to a nucleic acid-binding group, and cationic lipids or dendrimers as transfection agents. The invention also provides transfection comps. in which a peptide is covalently **linked** to the transfection agent (lipid, cationic lipid or dendrimer). Inclusion of peptides or modified-peptides in transfection comps. or covalent attachment of peptides to transfection agents results in enhanced transfection efficiency. Methods for the preparation of transfection comps. and methods of using these transfection comps. as intracellular delivery agents and extracellular targeting agents are also disclosed.

IC ICM C12N015-64

ICS C12N015-63; C12N007-00; C12N015-11

NCL 435458000

CC 3-2 (Biochemical Genetics)

ST peptide polycation **DNA** complex transformation efficiency;

polyamine peptide **DNA** complex transformation efficiency;

spermine peptide **DNA** complex transformation efficiency

IT **Proteins**, specific or class

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(BPI (bactericidal/permeability-increasing), increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(E5, peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(NLS (nuclear location signal sequence)-containing, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Lipids, biological studies

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(cationic, in transformation; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **DNA**

- RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(complexes, **conjugates**; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Peptides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(fusogenic, increasing efficiency of transformation with; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(hexon, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Cell adhesion molecules
Fibronectins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT RGD peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(increasing efficiency of transformation with; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Transformation, genetic
(increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Peptides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Hemagglutinins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(influenza virus, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT **Proteins**, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nucleic acid-binding, peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Alphavirus
Influenza virus
Vesicular stomatitis virus
(peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Amines, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(polyamines, nonpolymeric, complexes with **DNA**; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Animal cell
Fibroblast

- (transformation of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT Dendritic polymers
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(transformation using, increasing efficiency of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT Glycoproteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(viral, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT 92921-26-1, Sulfo-SMPB
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation spermine-containing peptides; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT 213131-54-5P 213131-55-6P 213131-56-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in preparation spermine-containing peptides; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT 213131-57-8 213131-71-6 213131-72-7 213131-74-9 213131-76-1 213131-78-3
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(increasing efficiency of transformation with; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT 71-44-3D, Spermine, peptide **conjugates**, complexes with nucleic acids 87695-40-7 95214-35-0 117138-20-2 127258-63-3 250252-75-6 264129-76-2 264129-83-1 264130-22-5 264130-52-1 264134-53-4 264134-54-5 264134-55-6 264134-56-7 264134-57-8 264134-58-9 264227-38-5
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT 2462-63-7, Lipofectace 104162-48-3, DOTMA 124050-77-7, DOGS 144189-73-1, DOTAP 158571-62-1, Lipofectamine 163442-69-1D, Starburst 6th generation, **conjugates** with lysine or arginine 163442-70-4D, Starburst 7th generation, **conjugates** with lysine or arginine 163442-72-6D, Starburst 9th generation, **conjugates** with lysine or arginine 168479-03-6, DOSPA 178532-92-8, DOSPER 189203-05-2, DMRIE-C 213131-59-0 213131-62-5 213131-65-8 213131-68-1 213131-69-2 213186-72-2, DMRIE-DOPE mixture 213252-20-1, Multifactor 213252-23-4, Superfect
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(transformation using, increasing efficiency of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT 264232-01-1 264252-63-3 264252-64-4 264252-65-5 264252-66-6 264252-67-7 264252-68-8 264252-69-9 264252-70-2 264252-72-4 264252-73-5 264252-74-6 264252-75-7 264252-76-8 264252-77-9 264252-78-0 264252-79-1 264252-80-4 264252-81-5 264252-82-6 264252-83-7 264252-84-8 264252-85-9 264252-86-0 264252-87-1

264261-81-6	264261-82-7	264261-83-8	264261-84-9	264261-85-0
264261-86-1	264261-87-2	264261-88-3	264261-90-7	264261-91-8
264261-92-9	264261-93-0	264261-94-1	264261-95-2	264261-96-3
264261-98-5	264261-99-6	264262-00-2	264262-02-4	264262-10-4
264262-18-2	264262-24-0	264262-30-8	264262-33-1	264262-37-5
264264-41-7	264264-66-6	264264-80-4	264264-91-7	264265-38-5
264266-32-2	264266-43-5	264266-59-3	264266-67-3	264271-84-3
264271-85-4	264271-86-5	264271-87-6	264272-18-6	264272-20-0

RL: PRP (Properties)

(unclaimed **protein** sequence; peptide-enhanced cationic lipid transfections)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:84648 CAPLUS

DOCUMENT NUMBER: 132:141941

TITLE: **Conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders

INVENTOR(S): Mcdonald, John R.; Coggins, Philip J.

PATENT ASSIGNEE(S): Osprey Pharmaceuticals Limited, Can.

SOURCE: PCT Int. Appl., 204 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004926	A2	20000203	WO 1999-CA659	19990721
WO 2000004926	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2335105	AA	20000203	CA 1999-2335105	19990721
AU 9948918	A1	20000214	AU 1999-48918	19990721
EP 1098664	A2	20010516	EP 1999-932572	19990721
EP 1098664	B1	20030806		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002521019	T2	20020716	JP 2000-560919	19990721
AT 246517	E	20030815	AT 1999-932572	19990721
EP 1346731	A1	20030924	EP 2003-76150	19990721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 2002168370	A1	20021114	US 2001-792793	20010222
HK 1037133	A1	20031107	HK 2001-107546	20011030
US 2003215421	A1	20031120	US 2003-375209	20030224

PRIORITY APPLN. INFO.:

US 1998-120523	A2	19980722
US 1998-155186P	P	19980722
EP 1999-932572	A3	19990721
WO 1999-CA659	W	19990721

US 1999-360242 A3 19990722
 US 1999-453851 A3 19991202
 US 2001-792793 A1 20010222

AB **Conjugates** containing as a ligand a chemokine receptor-targeting agent, such as chemokines, and a targeted agent, such as a toxin are provided. These **conjugates** are used to treat inflammatory responses associated with activation, proliferation and migration of immune effector cells, including leukocyte cell types, neutrophils, macrophages, and eosinophils. The **conjugates** provided herein are used to lessen or inhibit these processes to prevent or at least lessen the resulting secondary effects. In particular, the **conjugates** are used to target toxins to receptors on secondary tissue damage-promoting cells. The ligand moiety can be selected to deliver the cell toxin to such secondary tissue damage-promoting cells as mononuclear phagocytes, leukocytes, natural killer cells, dendritic cells, and T and B lymphocytes, thereby suppressing the proliferation, migration, or physiologic activity of such cells. Among preferred **conjugates** are fusion proteins having a chemokine, or a biologically active fragment thereof, as the ligand moiety linked to a cell toxin via a peptide linker of from 2 to about 60 amino acid residues.

IC ICM A61K047-48

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 15

ST antiinflammatory drug targeting fusion **protein** chemokine toxin sequence

IT AIDS (disease)

AIDS (disease)

(AIDS dementia complex; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Mental disorder

Mental disorder

(AIDS dementia; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines

RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (CTAP III, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Intestine, disease

(Crohn's; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines

RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (ENA-78, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines

RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (GCP-2, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

- IT Chemokines
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (GRO- α , **conjugates; conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (GRO- β , **conjugates; conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (GRP- γ , **conjugates; conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (IP-10, **conjugates; conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Kidney, disease
 (IgA nephropathy; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (LAPF-4, **conjugates; conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Lipoprotein receptors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (LDL; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (MIP-3, **conjugates; conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (Mig (monokine induced by interferon- γ), **conjugates; conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines

RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(NAP-2, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines

RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(PBP, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), bryodins, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), dianthin 30, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), dianthin 32, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), lychnin, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), mapalmin, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

- IT Barley
Corn
Flax
(RIP of; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Arthritis
(Reiter's syndrome; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(SDF-1 α (stromal-derived factor-1 α), **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(SDF-1 β (stromal-derived factor-1 β), **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(SDF-2, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Toxins
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(Shiga; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antitumor agents
(adenocarcinoma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Brain, disease
(adrenoleukodystrophy; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Respiratory distress syndrome
(adult; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Spinal column
(ankylosing spondylitis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Nutrients
(anti-; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antiarteriosclerotics

- (antiatherosclerotics; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Aspergillus
(aspergillosis from; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Astrocyte
Astrocyte
(astrocytoma, inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antitumor agents
(astrocytoma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Lung, disease
(bronchopulmonary dysplasia; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Nervous system
(central, inflammation; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Nervous system
(central, injury; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Fusion **proteins** (chimeric **proteins**)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chemokine receptor-binding; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(chemokine receptor-binding; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Leukocyte
(chemokine receptors of; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Meningitis
(chorio-; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Eye, disease
(choroiditis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Fatigue, biological
(chronic fatigue syndrome; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Intestine, disease
(colitis, chronic; **conjugates** and fusion **proteins**

for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Alzheimer's disease
 Anti-inflammatory agents
 Antiarthritics
 Antiparkinsonian agents
 Antirheumatic agents
 Antitumor agents
 Atherosclerosis
 B cell (lymphocyte)
 Basophil
 Behcet's syndrome
 Bronchodilators
 Cell migration
 Cell proliferation
 Coupling agents
 Dendritic cell
 Down's syndrome
 Drug targeting
 Encephalitis
 Encephalomyelitis
 Eosinophil
 Genetic vectors
 Granuloma
 Heart, disease
 Hodgkin's disease
 Immunosuppressants
 Inflammation
 Molecular cloning
 Multiple sclerosis
 Neutrophil
 Osteoarthritis
 Parkinson's disease
 Plasmid vectors
 Pneumonia
 Protein sequences
 Sarcoidosis
 T cell (lymphocyte)
 Venoms
 cDNA library
 cDNA sequences

(conjugates and fusion proteins for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Fusion proteins (chimeric proteins)
 RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (conjugates and fusion proteins for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Abrins
 Ricins
 Toxins
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (conjugates and fusion proteins for treating secondary tissue damage and other inflammatory conditions and disorders)

- disorders)
- IT Nucleic acids
 RL: BPN (Biosynthetic preparation); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Interleukin 3
 Macrophage inflammatory **protein 2**
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT G **protein**-coupled receptors
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Primers (nucleic acid)
 RL: PRP (Properties)
 (**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Trichosanthin
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Eotaxin
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Interleukin 1
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Interleukin 12
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Interleukin 13
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates** and fusion **proteins**

for treating secondary tissue damage and other inflammatory conditions and disorders)

- IT Interleukin 2
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates and fusion proteins**
 for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Interleukin 4
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates and fusion proteins**
 for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Interleukin 5
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates and fusion proteins**
 for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Interleukin 6
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates and fusion proteins**
 for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Interleukin 8
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates and fusion proteins**
 for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Macrophage inflammatory **protein 1 α**
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates and fusion proteins**
 for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Macrophage inflammatory **protein 1 β**
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates and fusion proteins**
 for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Monocyte chemoattractant **protein-1**
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (**conjugates; conjugates and fusion proteins**
 for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT RANTES (chemokine)
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP

(Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(**conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Neoplasm
(cytokine-regulated; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Nervous system
(degeneration; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Eye, disease
(diabetic retinopathy, proliferative; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(diphtheria; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Lung, disease
Pneumonia
(eosinophilic; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Pseudomonas
(exotoxin; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(exotoxins, of Pseudomonas; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Lung, disease
(fibrosis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fusion **proteins**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fusion-protein ligands for; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Neuroglia
Neuroglia

- (glioblastoma, inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antitumor agents
 - (glioblastoma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Neuroglia
 - Neuroglia
 - (glioma, inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antitumor agents
 - (glioma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Kidney, disease
 - (glomerulonephritis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Eye, disease
 - Joint, anatomical
 - Lung, disease
 - (inflammation; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Intestine, disease
 - (inflammatory; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Lung, neoplasm
 - Lung, neoplasm
 - (inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Drug delivery systems
 - (injections, i.m.; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Drug delivery systems
 - (injections, i.p.; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Drug delivery systems
 - (injections, i.v.; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Drug delivery systems
 - (injections, intraarticular; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Drug delivery systems
 - (injections, intracisternal; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Drug delivery systems
 - (injections, intradermal; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Drug delivery systems

- (injections, intraventricular; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Spinal cord
 - (injury; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Drug delivery systems
 - (intratracheal; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Rheumatoid arthritis
 - (juvenile; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antitumor agents
 - (leukemia; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Brain, disease
 - (leuko-; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Peptides, properties
 - RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
 - (**linkers**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Drug delivery systems
 - (local; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antitumor agents
 - Antitumor agents
 - (lung; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Kidney, disease
 - (lupus nephritis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antitumor agents
 - (lymphoma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
 - RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 - (macrophage inflammatory **protein**, γ , **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antitumor agents
 - (mammary gland; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antitumor agents
 - (melanoma; **conjugates** and fusion **proteins** for

- treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Meninges
(meningioma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Neuroglia
(microglia, microglioma inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(momordins, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antibodies
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(monoclonal; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monocyte chemoattractant **protein 3**, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monocyte chemoattractant **protein 4**, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monocyte chemoattractant **protein 5**, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monocyte chemoattractant **protein-2**, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Phagocyte
(mononuclear; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Antitumor agents
(myeloma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

- IT Lymphocyte
(natural killer cell; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions
and disorders)
- IT Mammary gland
Mammary gland
Prostate gland
Prostate gland
(neoplasm, inhibitors; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions
and disorders)
- IT Kidney, disease
(nephritis; **conjugates** and fusion **proteins** for
treating secondary tissue damage and other inflammatory conditions and
disorders)
- IT Neuroglia
Neuroglia
(oligodendroglioma, inhibitors; **conjugates** and fusion
proteins for treating secondary tissue damage and other
inflammatory conditions and disorders)
- IT Antitumor agents
(oligodendroglioma; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions
and disorders)
- IT Drug delivery systems
(ophthalmic; **conjugates** and fusion **proteins** for
treating secondary tissue damage and other inflammatory conditions and
disorders)
- IT Nose
(polyposis; **conjugates** and fusion **proteins** for
treating secondary tissue damage and other inflammatory conditions and
disorders)
- IT Antitumor agents
(prostate gland; **conjugates** and fusion **proteins** for
treating secondary tissue damage and other inflammatory conditions and
disorders)
- IT Arthritis
(psoriatic arthritis; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions
and disorders)
- IT Arthritis
(reactive; **conjugates** and fusion **proteins** for
treating secondary tissue damage and other inflammatory conditions and
disorders)
- IT Eye, disease
(retinitis; **conjugates** and fusion **proteins** for
treating secondary tissue damage and other inflammatory conditions and
disorders)
- IT Nose
(rhinitis; **conjugates** and fusion **proteins** for
treating secondary tissue damage and other inflammatory conditions and
disorders)
- IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); PEP (Physical, engineering or chemical process); THU
(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(saporins, **conjugates**; **conjugates** and fusion
proteins for treating secondary tissue damage and other
inflammatory conditions and disorders)
- IT Antitumor agents

- (sarcoma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Eye, disease
 - (scleritis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Respiratory tract
 - (sinusitis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Venoms
 - (snake; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Spinal column
 - (spondyloarthropathy; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Brain, disease
 - (spongiform encephalopathy; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Brain, disease
 - (stroke; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Drug delivery systems
 - (targeted; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Thyroid gland, disease
 - (thyroiditis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Drug delivery systems
 - (topical; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Bacteria (Eubacteria)*
 - Insect (Insecta)
 - Plant (Embryophyta)
 - Spider
 - (toxins of; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Intestine, disease
 - (ulcerative colitis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Biological transport
 - (uptake; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Eye, disease
 - (uveitis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Glycoproteins, specific or class
 - RL; BAC (Biological activity or effector, except adverse); BSU (Biological

- study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(α -momorcharins, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Macroglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(α 2-; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT Glycoproteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(β -momorcharins; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT 51-17-2, Benzimidazole 84-65-1, Anthraquinone 120500-15-4, Leinamycin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA-cleaving; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT 256633-15-5P
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT 50-07-7, Mitomycin c 51-21-8, 5-Fluorouracil 55-86-7, Nitrogen mustard 59-05-2, Methotrexate 148-82-3, Melphalan 11000-04-7D, Colicin, **conjugates** 20830-81-3, Daunomycin 23214-92-8, Doxorubicin 65988-88-7, Modeccin 75037-46-6D, Gelonin, **conjugates** 91933-11-8, Volkensin 95787-44-3D, Dodecandrin, **conjugates** 160674-53-3D, Luffin a, **conjugates** 160674-54-4D, Luffin b, **conjugates**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT 9003-98-9, Dnase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
- IT 81627-83-0, Mcsf 83869-56-1, Gmcsf 143011-72-7, Gcsf
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions

- and disorders)
- IT 69-78-3 15791-08-9 68181-17-9 72252-96-1 88442-68-6,
S-(2-Pyridylthio)-L-cysteine **106145-13-5** 115616-51-8
150244-18-1 158913-22-5 160854-54-6 199804-25-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(cross-linker; **conjugates** and fusion
proteins for treating secondary tissue damage and other
inflammatory conditions and disorders)
- IT 256633-14-4P
RL: BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological
study); PREP (Preparation)
(**nucleotide** sequence; **conjugates** and fusion
proteins for treating secondary tissue damage and other
inflammatory conditions and disorders)
- IT 203780-20-5 225895-00-1 256633-43-9, 7: PN: WO0004926 SEQID: 40
unclaimed **DNA** 256633-44-0, 8: PN: WO0004926 SEQID: 41
unclaimed **DNA** 256633-45-1, 9: PN: WO0004926 SEQID: 42
unclaimed **DNA** 256633-46-2 256633-47-3 256633-48-4
256633-49-5 256633-50-8 256633-51-9 256633-52-0 256633-53-1
256633-54-2 256633-55-3 256633-56-4 256633-57-5 256633-58-6
256633-59-7 256633-60-0 256633-61-1 256633-62-2 256633-63-3
256633-64-4 256633-65-5 256633-66-6 256633-67-7 256633-68-8
256633-69-9
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; **conjugates** and
fusion **proteins** for treating secondary tissue damage and
other inflammatory conditions and disorders)
- IT 2543-43-3 99283-10-0, Colony-stimulating factor 2 (human clone pHG25
protein moiety reduced) 102619-52-3, Lymphokine MIP 1 α
(human clone pLD78 macrophage inflammatory reduced) 104950-39-2,
Interleukin 4 (human clone 46 **protein** moiety reduced)
111906-18-4, Interleukin 3 (human clone D11 **protein** moiety
reduced) 112002-52-5, Toxin (Shigella dysenteriae A-subunit reduced)
112487-62-4, Interleukin 8 (human clone 3-10C reduced) 112871-94-0,
Toxin SLT-II (bacteriophage 933W A-subunit precursor reduced)
117216-60-1, **Protein** (human T-lymphocyte gene RANTES reduced)
118899-93-7, Melanoma growth stimulatory activity (human clone pMGSA5-2/3
isoform α reduced) 121853-02-9, Lymphokine MIP 1 β (human
clone pAT744 macrophage inflammatory reduced) 124147-31-5, Lymphokine
MCP 1 (human **protein** moiety reduced) 124760-57-2,
Protein MAP (Mirabilis jalapa clone pMH2 reduced) 128794-97-8,
Trichosanthin (Trichosanthes kirilowii strain Maximowicz) 130838-28-7
131199-57-0, Lymphokine MIP 2 β (human clone hMIP-2-4a macrophage
inflammatory reduced) 131199-58-1, Lymphokine MIP 2 α (human clone
hMIP-2-5a macrophage inflammatory reduced) 141961-54-8, **Protein**
(human sialoglycoprotein LRP-associated) 143973-96-0, Cytokine (human
clone NC28 **protein** moiety reduced) 150243-58-6 150243-59-7
153177-60-7 188204-50-4, 24-270-Bryodin 1 (Bryodin dioica) 189582-41-0
189704-25-4, Eotaxin (human clone pVL141) 194675-15-5, Dendrokinine (human
clone SHO46) 197665-51-3 256633-70-2 256633-71-3 256633-72-4
256633-73-5 256649-82-8 256649-85-1
RL: PRP (Properties)
(unclaimed **protein** sequence; **conjugates** and fusion
proteins for treating secondary tissue damage and other
inflammatory conditions and disorders)
- IT 256504-33-3 256504-34-4 256504-35-5 256504-36-6 256504-37-7
RL: PRP (Properties)
(unclaimed sequence; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions
and disorders)

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TITLE: A Multistep Chemical Modification Procedure To Create
DNA Arrays on Gold Surfaces for the Study of
Protein-DNA Interactions with
 Surface Plasmon Resonance Imaging

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AB A multistep surface modification procedure for the creation of DNA arrays on chemical modified gold surfaces that can be used in surface plasmon resonance (SPR) imaging studies of protein-DNA interactions is demonstrated. The multistep procedure is required to create an array of spots that are surrounded first by a hydrophobic background which allows for the pinning of aqueous DNA solns. onto individual array elements and then to replace that hydrophobic background with one that resists the nonspecific adsorption of proteins during in situ SPR imaging measurements. An **amine**-terminated alkanethiol monolayer is employed as the base layer, and Fmoc and PEG **modifiers** are used to create the sequentially hydrophobic and protein adsorption-resistant surfaces, resp. Specifically, the chemical **modification** steps are the following: (1) the adsorption and self-assembly of an 11-mercaptoundecylamine (MUAM) monolayer on an evaporated gold thin film, (2) the reaction of the MUAM monolayer with an Fmoc protecting group to create a hydrophobic surface, (3) the photopatterned removal of the alkanethiol followed by (4) the readsorption of MUAM to create an array of MUAM squares (750+750 μ m) surrounded by a hydrophobic MUAM-Fmoc background that can pin drops of aqueous solution, (5) the attachment of **oligonucleotide** sequences onto the MUAM squares by the reaction of the **amine**-terminated surface with the heterobifunctional cross linker SSMCC followed by a coupling reaction to a small volume (0.1 μ L) of thiol-**modified** DNA, and (6) the removal of the Fmoc protecting group followed by (7) a pegylation reaction of the MUAM with PEG-NHS to create a protein adsorption-resistant background. A combination of polarization-modulation FTIR spectroscopy, contact angle, and scanning angle SPR measurements is used to characterize the surface modification procedure. An SPR imaging measurement of the adsorption of single-stranded DNA binding protein (SSB) onto an oligonucleotide array created by this procedure is used to demonstrate the utility of these surfaces.

CC 9-1 (Biochemical Methods)

Section cross-reference(s): 6.

ST DNA array chip **protein** recognition surface plasmon
 resonance imaging

IT Analytical apparatus

(DNA arrays on gold surface, supported by silanized
 microscope slide covers; multistep chemical modification procedure to
 create DNA arrays on gold surfaces for study of
protein-DNA interactions with surface plasmon
 resonance imaging)

IT **Proteins**, specific or class

RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
 (SSB (single-stranded **DNA**-binding); multistep chemical
 modification procedure to create **DNA** arrays on gold surfaces
 for study of **protein-DNA** interactions with surface
 plasmon resonance imaging)

IT Imaging
 Molecular recognition
 Self-assembled monolayers
 (multistep chemical modification procedure to create **DNA** arrays
 on gold surfaces for study of **protein-DNA**
 interactions with surface plasmon resonance imaging)

IT **Proteins**, general, analysis
 RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
 (multistep chemical modification procedure to create **DNA** arrays
 on gold surfaces for study of **protein-DNA**
 interactions with surface plasmon resonance imaging)

IT **DNA**
 RL: ARG (Analytical reagent use); DEV (Device component use); ANST
 (Analytical study); USES (Uses)
 (multistep chemical modification procedure to create **DNA** arrays
 on gold surfaces for study of **protein-DNA**
 interactions with surface plasmon resonance imaging)

IT **Oligonucleotides**
 RL: ARG (Analytical reagent use); DEV (Device component use); ANST
 (Analytical study); USES (Uses)
 (multistep chemical modification procedure to create **DNA** arrays
 on gold surfaces for study of **protein-DNA**
 interactions with surface plasmon resonance imaging)

IT Adsorption
 (**protein**; multistep chemical modification procedure to create
DNA arrays on gold surfaces for study of **protein-**
DNA interactions with surface plasmon resonance imaging)

IT Surface plasmon
 (resonance; multistep chemical modification procedure to create
DNA arrays on gold surfaces for study of **protein-**
DNA interactions with surface plasmon resonance imaging)

IT 247247-38-7 247247-40-1
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (multistep chemical modification procedure to create **DNA** arrays
 on gold surfaces for study of **protein-DNA**
 interactions with surface plasmon resonance imaging)

IT 7440-57-5, Gold, uses
 RL: DEV (Device component use); USES (Uses)
 (multistep chemical modification procedure to create **DNA** arrays
 on gold surfaces for study of **protein-DNA**
 interactions with surface plasmon resonance imaging)

IT 82911-69-1 103708-09-4, **Sulfo-SMCC**
 130727-41-2 155638-19-0
 RL: DEV (Device component use); RCT (Reactant); RACT (Reactant or
 reagent); USES (Uses)
 (multistep chemical modification procedure to create **DNA** arrays
 on gold surfaces for study of **protein-DNA**
 interactions with surface plasmon resonance imaging)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1998:719089 CAPLUS
 DOCUMENT NUMBER: 129:341449
 TITLE: Active microtubule-based separations by kinesins

INVENTOR(S): Stewart, Russell J.
 PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
 SOURCE: U.S., 24 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5830659	A	19981103	US 1996-713815	19960913
PRIORITY APPLN. INFO.:			US 1996-713815	19960913

AB A method and system for separating a selected mol. from a heterogeneous mixture of mols. in aqueous solution are described. The method comprises (a) providing a separation device comprising a loading reservoir and a receiving reservoir coupled by a channel bearing immobilized microtubules aligned parallel to the longitudinal axis of the channel; (b) placing an aqueous solution containing the heterogeneous mixture of mols. in the loading reservoir; (c) adding a motor-ligand composition and ATP to the aqueous solution, wherein the composition comprises a motor protein for attaching to microtubules and moving therealong in the presence of ATP and the ligand is capable of binding the selected mol., such that the ligand binds the selected mol. to form a complex and the complex moves along the immobilized microtubules to the receiving reservoir; and (d) removing the selected mol. from the receiving chamber. Thus, a separation device was prepared by photolithog. etching of a glass substrate. The channel separating the loading and receiving chambers was derivatized with trimethoxysilylpropyldiethylenetriamine. A fraction of the surface amino groups were then reacted with **sulfosuccinimidyl** -(4-azidosalicylamido)-hexanoate. Microtubules were aligned in the channel by flow alignment. Microtubules electrostatically bound to the channel surface were crosslinked to the surface by UV irradiation. Then a solution containing ATP and phage λ and plasmid pBR322 was placed in the reservoir. A kinesin-cos site-binding oligonucleotide conjugate was then added to the reservoir. There was separation of λ DNA from pBR322 DNA because active transport of λ DNA to the receiving reservoir is more rapid than diffusion of the pBR322 DNA.

IC ICM C12Q001-68
 ICS C12Q001-34; G01N033-566; C12M001-40
 NCL 435006000
 CC 9-9 (Biochemical Methods)
 IT **Oligonucleotides**
 RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); BIOL (Biological study); PROC (Process); USES (Uses)
 (conjugates with motor proteins; active microtubule-based sepns. by kinesins)

IT 215378-84-0D, **conjugates with oligonucleotides** and fusion proteins with streptavidin 215378-85-1D, **conjugates with oligonucleotides** and fusion proteins with streptavidin
 RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); BIOL (Biological study); PROC (Process); USES (Uses)
 (amino acid sequence; active microtubule-based sepns. by kinesins)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:621324 CAPLUS
 DOCUMENT NUMBER: 129:240848
 TITLE: Increasing the efficiency of uptake of transforming
 DNA complexes with polycations using peptides
 INVENTOR(S): Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen;
 Jessee, Joel A.; Ciccarone, Valentina C.; Evans,
 Krista L.; Schifferli, Kevin P.; Gebeyehu, Guililat
 PATENT ASSIGNEE(S): Life Technologies, Inc., USA
 SOURCE: PCT Int. Appl., 105 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840502	A1	19980917	WO 1998-US5232	19980316
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6051429	A	20000418	US 1997-818200	19970314
AU 9865622	A1	19980929	AU 1998-65622	19980316
EP 1007699	A1	20000614	EP 1998-911737	19980316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001517939	T2	20011009	JP 1998-539899	19980316
PRIORITY APPLN. INFO.: US 1997-818200 A 19970314 US 1995-477354 B2 19950607 US 1996-658130 A2 19960604 WO 1998-US5232 W 19980316				

AB A method of increasing the efficiency of transformation of eukaryotic cells using complexes of nucleic acids with polycations is described. The method uses peptide **conjugates** with nucleic acid-binding moieties, cationic lipids and dendrimers to complex the DNA. The peptides may be synthetic or derived from a cellular protein and may be further derivatized, e.g. by selective deprotection. The peptide may also be covalently **linked** to the transfection agent (lipid, cationic lipid or dendrimer). Inclusion of peptides or modified-peptides in transfection compns. or covalent attachment of peptides to transfection agents increases the efficiency of transfection. Methods for the preparation of transfection compns. and methods of using these transfection compns. as intracellular delivery agents and extracellular targeting agents are also disclosed.

IC ICM C12N015-64

ICS C12N015-63; C07K014-00; G01N033-92

CC 3-1 (Biochemical Genetics)

ST peptide polycation **DNA** complex transformation efficiency;
 polyamine peptide **DNA** complex transformation efficiency;
 spermine peptide **DNA** complex transformation efficiency

IT **Proteins**, specific or class

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(Uses)

(BPI (bactericidal/permeability-increasing), increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT Glycoproteins, specific or class

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(Semliki forest virus, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT Toxins

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(Shiga, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT Proteins, specific or class

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(VP22, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT Lipids, biological studies

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(cationic, in transformation; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT DNA

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(complexes, conjugates; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT Toxins

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(diphtheria, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT Toxins

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(endotoxins, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT Peptides, biological studies

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(fusogenic, increasing efficiency of transformation with; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT Antigens

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(hepatitis B core, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT Proteins, specific or class

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(hexon, increasing efficiency of transformation with peptides of;

- increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Cell adhesion molecules
 - Fibronectins
 - High-mobility group **proteins**
 - Histones
 - Lactoferrins
 - Transferrins
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Transformation, genetic
 - (increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Peptides, biological studies
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Hemagglutinins
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (influenza virus, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT **Proteins**, specific or class
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (internalins, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT **Proteins**, specific or class
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (invasins, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT **Proteins**, specific or class
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (knob, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT **Proteins**, specific or class
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (nucleic acid-binding, peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT **Proteins**, specific or class
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (penton base, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
- IT Receptors
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (peptides and ligands of, increasing efficiency of transformation with; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

- IT Adenoviridae
 - Alphavirus
 - Hepatitis virus
 - Herpesviridae
 - Human immunodeficiency virus
 - Influenza virus
 - Semliki Forest virus*
 - Vesicular stomatitis virus
 - (peptides of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT Polyamines
 - Polyamines
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (polyamide-, transformation using, increasing efficiency of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT Polyamides, biological studies
 - Polyamides, biological studies
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (polyamine-, transformation using, increasing efficiency of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT Amines, biological studies
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (polyamines, nonpolymeric, complexes with DNA; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT Transcription factors
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (tat, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT Protamines
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (thionins, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT Animal cell
 - Fibroblast
 - (transformation of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT Dendritic polymers
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (transformation using, increasing efficiency of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT 92921-26-1, Sulfo-SMPB
 - RL: RCT (Reactant); RACT (Reactant or reagent)
 - (in preparation spermine-containing peptides; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)
- IT 213131-54-5P 213131-55-6P 213131-56-7P
 - RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(in preparation spermine-containing peptides; increasing efficiency of uptake of

transforming DNA complexes with polycations using peptides)

IT 9004-10-8D, Insulin, peptides, biological studies 62031-54-3D, Fibroblast growth factor, peptides 62229-50-9D, Epidermal growth factor, peptides

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(increasing efficiency of transformation with; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT 1405-97-6D, Gramicidin, peptides 1414-45-5D, Nisin, derivs., peptides 37231-28-0D, Melittin, derivs., peptides 80802-79-5D, Cecropin, peptides 103220-14-0D, Defensin, peptides 113041-69-3D, Magainin, derivs., peptides 116229-36-8D, Bactenecin, derivs., peptides 123997-21-7D, Apidaecin, derivs., peptides 140896-21-5D, Indolicidin, derivs., peptides 148045-87-8D, Tachyplesin, peptides 163663-18-1D, Protegrin, peptides 170006-50-5D, Cathelicidin, derivs., peptides 173010-28-1D, Buforin I, derivs., peptides 182970-24-7D, Drosomycin, derivs., peptides 213131-57-8 213131-71-6 213131-72-7 213131-74-9 213131-76-1 213131-78-3

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(increasing efficiency of transformation with; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT 71-44-3D, Spermine, peptide **conjugates**, complexes with nucleic acids

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

IT 2462-63-7, Lipofectace 124050-77-7, DOGS 158571-62-1, Lipofectamine 163442-69-1D, Starburst 6th generation, **conjugates** with lysine or arginine 163442-70-4D, Starburst 7th generation, **conjugates** with lysine or arginine 163442-72-6D, Starburst 9th generation, **conjugates** with lysine or arginine 168479-03-6, DOSPA 178532-92-8, DOSPER 189203-04-1, Cellfectin 189203-05-2, DMRIE-C 213131-59-0 213131-62-5 213131-65-8 213131-68-1 213131-69-2 213186-72-2, DMRIE-DOPE mixture 213252-20-1, Multifector 213252-23-4, Superfect

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(transformation using, increasing efficiency of; increasing efficiency of uptake of transforming DNA complexes with polycations using peptides)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:572338 CAPLUS

DOCUMENT NUMBER: 129:186415

TITLE: Detection of targets with green fluorescent **protein** and fluorescent variants thereof

INVENTOR(S): Plaia, Todd W.

PATENT ASSIGNEE(S): Oncor, Inc., USA

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9836099	A1	19980820	WO 1998-US3147	19980218
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9866588	A1	19980908	AU 1998-66588	19980218
EP 1000172	A1	20000517	EP 1998-908588	19980218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001514741	T2	20010911	JP 1998-536010	19980218
PRIORITY APPLN. INFO.: US 1997-38623P P 19970218				
WO 1998-US3147 W 19980218				
AB	A labeled marker for detection of a target is described which includes a label selected from the group consisting of green fluorescent protein and a fluorescent variant thereof, and a ligand configured to bind to the target. The ligand includes any mol. or combination of mols. which have an affinity for another substance. For example, the ligand can be selected from the group consisting of nucleic acid probe, antibody, hapten conjugate , biotin, avidin and streptavidin. A method for detecting a target is also described which includes providing a primary ligand configured to bind to the target and providing a secondary ligand configured to bind to the primary ligand. Techniques such as fluorescent microscopy are used to visualize the labeled marker.			
IC	ICM C12Q001-68 ICS G01N033-53; C12P021-04; C12N009-02; C07K001-00; C07H019-04; C07H021-04			
CC	9-5 (Biochemical Methods) Section cross-reference(s): 3, 6			
ST	green fluorescent protein ligand marker binding; fluorescence green fluorescent protein ligand marker			
IT	Azides RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses) (aryl; detection of targets with green fluorescent protein and fluorescent variants thereof)			
IT	Gene, animal RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence) (c-erbB2; detection of targets with green fluorescent protein and fluorescent variants thereof)			
IT	Ligands RL: ARG (Analytical reagent use); ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses) (conjugated , with green fluorescent protein variants; detection of targets with green fluorescent protein and fluorescent variants thereof)			
IT	Avidins Haptens RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL			

- (Biological study); PROC (Process)
 - (**conjugates**, with green fluorescent **protein**;
 - detection of targets with green fluorescent **protein** and fluorescent variants thereof)
- IT Staining, biological
 - (counterstain; detection of targets with green fluorescent **protein** and fluorescent variants thereof)
- IT **Crosslinking**
 - ~~Crosslinking agents~~
 - Fluorescent probes
 - Fluorescent substances
 - Fluorometry
 - Genetic mapping
 - Immunoassay
 - Molecular association
 - Nucleic acid hybridization
 - (detection of targets with green fluorescent **protein** and fluorescent variants thereof)
- IT Carbohydrates, analysis
 - DNA
 - Proteins, general, analysis
 - RNA
 - RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
 - (detection of targets with green fluorescent **protein** and fluorescent variants thereof)
- IT Alkyl halides
 - RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 - (detection of targets with green fluorescent **protein** and fluorescent variants thereof)
- IT Aryl halides
 - RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 - (detection of targets with green fluorescent **protein** and fluorescent variants thereof)
- IT **Proteins**, specific or class
 - RL: ARG (Analytical reagent use); ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 - (green fluorescent; detection of targets with green fluorescent **protein** and fluorescent variants thereof)
- IT Acetals
 - RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 - (halo-; detection of targets with green fluorescent **protein** and fluorescent variants thereof)
- IT Chromosome
 - (human 17; detection of targets with green fluorescent **protein** and fluorescent variants thereof)
- IT Chromosome
 - (human Y; detection of targets with green fluorescent **protein** and fluorescent variants thereof)
- IT Esters, analysis
 - RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological

study); RACT (Reactant or reagent); USES (Uses)
(imides; detection of targets with green fluorescent **protein**
and fluorescent variants thereof)

IT Nucleic acid hybridization
(in situ, fluorescence; detection of targets with green fluorescent
protein and fluorescent variants thereof)

IT Nucleic acid hybridization
(in situ; detection of targets with green fluorescent **protein**
and fluorescent variants thereof)

IT Antibodies

Probes (nucleic acid)

RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU
(Biological study, unclassified); ANST (Analytical study); BIOL
(Biological study); PROC (Process)

(labeled with green fluorescent **protein**; detection of targets
with green fluorescent **protein** and fluorescent variants
thereof)

IT Fluorescent indicators
(marker; detection of targets with green fluorescent **protein**
and fluorescent variants thereof)

IT 25535-16-4, Propidium iodide 47165-04-8, DAPI
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(detection of targets with green fluorescent **protein** and
fluorescent variants thereof)

IT 58-85-5D, Biotin, labeled with green fluorescent **protein**
1672-46-4, Digoxigenin 9013-20-1D, Streptavidin, labeled with green
fluorescent **protein**
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU
(Biological study, unclassified); ANST (Analytical study); BIOL
(Biological study); PROC (Process)
(detection of targets with green fluorescent **protein** and
fluorescent variants thereof)

IT 107-22-2, Glyoxal 151-51-9, Carbodiimide 541-59-3, Maleimide
6066-82-6D, N-Hydroxysuccinimide, esters 35013-72-0, Biotin
N-hydroxysuccinimide ester 73370-52-2, Pyridine, dithiobis 76931-93-6,
N-Succinimidyl S-acetylthioacetate 103708-09-4, Sulfo-
SMCC
RL: ARU (Analytical role, unclassified); BUU (Biological use,
unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological
study); RACT (Reactant or reagent); USES (Uses)
(detection of targets with green fluorescent **protein** and
fluorescent variants thereof)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:475105 CAPLUS

DOCUMENT NUMBER: 127:106361

TITLE: Preparation of photoprotein **conjugates** and
methods of use thereof

INVENTOR(S): Stults; Nancy L.

PATENT ASSIGNEE(S): Sealite Sciences, Inc., USA

SOURCE: U.S., 21 pp., Cont.-in-part of U.S. 5,486,455.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5648218	A	19970715	US 1995-465791	19950606
US 5486455	A	19960123	US 1994-293648	19940822
PRIORITY APPLN. INFO.:			US 1993-117116	B1 19930813
			US 1994-293648	A2 19940822
			US 1993-17116	B1 19930212

AB The present invention encompasses a method of synthesis of **conjugates** of photoproteins that retain all or a substantial portion of the luminescent activity of underivatized photoprotein. According to the present invention photoproteins may be **conjugated** with a variety of binding reagents including streptavidin/avidin, glycoproteins, lectins, hormones, antigens, drugs, antibodies and antigen-binding fragments thereof, or any other selectively bindable reagent by chemical **crosslinking** means. The present invention also encompasses **conjugates** produced by this method and methods of use of such **conjugates**.

IC ICM C12Q001-68
ICS C12Q001-70; G01N033-53; C07H021-04

NCL 435006000

CC 9-15 (Biochemical Methods)

ST aequorin **conjugate**; avidin photoprotein **conjugate**; glycoprotein photoprotein **conjugate**; lectin photoprotein **conjugate**; hormone photoprotein **conjugate**; antigen photoprotein **conjugate**; antibody photoprotein **conjugate**; drug photoprotein **conjugate**

IT Aequorins
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
RACT (Reactant or reagent); USES (Uses)
(apoequorins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
RACT (Reactant or reagent); USES (Uses)
(apoberovins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
RACT (Reactant or reagent); USES (Uses)
(apomnemioipsins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
RACT (Reactant or reagent); USES (Uses)
(apoobelins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
RACT (Reactant or reagent); USES (Uses)
(clytins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
RACT (Reactant or reagent); USES (Uses)
(halistovein thalassiciolins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
RACT (Reactant or reagent); USES (Uses)
(mnemiopsins; preparation of photoprotein **conjugates** and methods of use thereof)

- IT **Proteins**, specific or class
 RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
 RACT (Reactant or reagent); USES (Uses)
 (obelins; preparation of photoprotein **conjugates** and methods of use thereof)
- IT **Proteins**, specific or class
 RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
 RACT (Reactant or reagent); USES (Uses)
 (photoproteins; preparation of photoprotein **conjugates** and methods of use thereof)
- IT Aequorins
 Agglutinins and Lectins
 Antibodies
 Antigens
 Avidins
 Drugs
 Enzymes, reactions
 Glycoproteins, specific or class
 Hormones, animal, reactions
 Oligonucleotides
 Peptides, reactions
 Receptors
 RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
 RACT (Reactant or reagent); USES (Uses)
 (preparation of photoprotein **conjugates** and methods of use thereof)
- IT 9013-20-1, Streptavidin 96827-88-2, Pholasin
 RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
 RACT (Reactant or reagent); USES (Uses)
 (preparation of photoprotein **conjugates** and methods of use thereof)
- IT 4856-87-5, Bis(maleimido)hexane 6539-14-6, 2-Iminoethiolane 6953-60-2,
 S-Acetylmercaptosuccinic anhydride 15209-14-0, Bis(maleimido) methyl
 ether 58626-38-3 64987-85-5, SMCC 79886-55-8 80307-12-6, GMBS
 83306-17-6, N-Succinimidyl-3-(2-pyridylthio)propionate 92921-26-1
 , Sulfo-SMPB 103708-09-4, Sulfo-
 SMCC 185332-92-7, Sulfo-GMBS
 RL: NUU (Other use, unclassified); USES (Uses)
 (preparation of photoprotein **conjugates** and methods of use thereof)

L31 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1997:130043 CAPLUS
 DOCUMENT NUMBER: 126:127859
 TITLE: Use of biologically active peptides to increase the
 efficiency of transformation with **DNA**
 :cationic lipid complexes
 INVENTOR(S): Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen;
 Jessee, Joel A.; Schifferli, Kevin P.
 PATENT ASSIGNEE(S): Life Technologies, Inc., USA; Hawley-Nelson, Pamela;
 Lan, Jianqing; Shih, Pojen; Jessee, Joel A.;
 Schifferli, Kevin P.
 SOURCE: PCT Int. Appl., 64 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9640961      A1      19961219      WO 1996-US8723      19960604
W:  AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,
    ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS,
    LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
    SE, SG
RW:  AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AU 9659792      A1      19961230      AU 1996-59792      19960604
EP 874910       A1      19981104      EP 1996-917118      19960604
R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
    IE, SI, LT, LV, FI
JP 11506935     T2      19990622      JP 1996-501227      19960604
RITY-APPLN. INFO.:  * * * * * US 1995-477354      A      19950607
WO 1996-US8723      W      19960604

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AB Biol. active peptides, such as receptor ligands, fusogenic peptides, or nuclear localization signals are incorporated into complexes of DNA and cationic lipids to increase the effectiveness of transformation of eukaryotic cells. These peptides may also be **conjugated** with a DNA-binding peptide or group such as spermine. Methods for the preparation of transfecting compns. and use as intracellular delivery agents and extracellular targeting agents are also disclosed. Transformation efficiencies of animal cell lines with LipofectAMINE® liposomes were increased by up to .apprx.50-fold when **conjugates** of viral RGD peptides and spermine were added to the complex.

IC ICM C12N015-88
ICS C12N007-04; C07H021-00

CC 3-1 (Biochemical Genetics)

IT Glycoproteins, specific or class

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HN (hemagglutinin-neuraminidase), fusogenic peptides of; use of biol.
active peptides to increase efficiency of transformation with
DNA:cationic lipid complexes)

IT Proteins, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(NLS (nuclear location signal sequence)-containing, peptides of, in liposome transformations; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT Lipids, biological studies

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(cationic and neutral, transformation with liposomes containing; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)

IT Alphavirus

Influenza virus

Vesicular stomatitis virus

(fusogenic peptides of; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT Peptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(fusogenic, in liposome transformations; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)

IT Antigens

- RL: BSU (Biological study, unclassified); BIOL (Biological study)
(large T, nuclear localization peptides of; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)
- IT Simian virus 40
(nuclear localization peptides of; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)
- IT Transformation, genetic
(of eukaryotic cells; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)
- IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptide ligands for, in liposome transformations; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)
- IT Amines, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(polyamines, nonpolymeric, effects on LipofectAMINE-mediated transformation efficiency of; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)
- IT Fibroblast
(transformation of; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)
- IT 71-44-3D, Spermine, peptide conjugates
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(DNA binding by; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)
- IT 95214-35-0 117138-20-2 127258-60-0 127258-63-3
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence, effects on LipofectAMINE-mediated transformation efficiency of; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)
- IT 186451-48-9P 186451-51-4P 186451-54-7P 186451-56-9P
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence, effects on LipofectAMINE-mediated transformation efficiency of; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)
- IT 92921-26-1, Sulfo-SMPB
RL: RCT (Reactant); RACT (Reactant or reagent)
(crosslinking of peptides and spermine using; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)
- IT 25104-18-1, Polylysine 38000-06-5, Polylysine
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(effects on LipofectAMINE-mediated transformation efficiency of; use of biol. active peptides to increase efficiency of transformation with DNA:cationic lipid complexes)
- IT 186451-46-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation and reactions of, in **conjugation of proteins** with spermine; use of biol. active peptides to increase efficiency of transformation with **DNA:cationic lipid complexes**)

IT 2462-63-7, Dioleoylphosphatidylethanolamine 185097-43-2

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(transformation with liposomes containing; use of biol. active peptides to increase efficiency of transformation with **DNA:cationic lipid complexes**)

IT 158571-62-1, Lipofectamine

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(transformation with; use of biol. active peptides to increase efficiency of transformation with **DNA:cationic lipid complexes**)

L31 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:610222 CAPLUS

DOCUMENT NUMBER: 125:269866

TITLE: CAP-phenanthroline conjugate for DNA cleavage

INVENTOR(S): Ebright, Richard H.; Ebright, Y. W.; Pendergrast, P. Shannon

PATENT ASSIGNEE(S): Rutgers University, USA

SOURCE: U.S., 12 pp., Cont. of U.S. Ser. No. 124,362, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5556949	A	19960917	US 1994-320568	19941011
PRIORITY APPLN. INFO.:			US 1991-747731	19910820
			US 1993-124362	19930920

OTHER SOURCE(S): MARPAT 125:269866

AB A class of site-specific **DNA** cleavage agents is disclosed comprising a sequence-specific **DNA**-binding protein (i.e., catabolite gene-activator protein, CAP) and a nucleolytic moiety (i.e., 1,10-phenanthroline derivative) attached thereto at an **amino acid** that is close to **DNA** in the specific protein-**DNA** complex but that is not close to **DNA** in the nonspecific protein-**DNA** complex. These site-specific **DNA** cleavage agents cleave **DNA** at specific **DNA** recognition sites and have little or no nonspecific **DNA** cleavage activity.

IC ICM C07K001-107

ICS C07D471-02; C12Q001-68

NCL 530402000

CC 9-15 (Biochemical Methods)

Section cross-reference(s): 3, 6, 67

ST **DNA** cleavage agent CAP phenanthroline **conjugate**; catabolite gene activator **protein DNA** cleavage

IT Ribonucleic acid formation factors

RL: BPR (Biological process); BSU (Biological study, unclassified); CAT (Catalyst use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(CAP (catabolite gene activator **protein**), **conjugates** with phenanthroline derivs.; CAP-phenanthroline **conjugate** for

DNA cleavage)

- IT 182685-69-4DP, CAP **protein conjugates** 182685-70-7DP,
CAP **protein conjugates** 182685-71-8DP, CAP
protein conjugates
RL: BPR (Biological process); BSU (Biological study, unclassified); CAT
(Catalyst use); SPN (Synthetic preparation); BIOL (Biological study); PREP
(Preparation); PROC (Process); USES (Uses)
(CAP-phenanthroline **conjugate** for DNA cleavage)
- IT 598-21-0, Bromoacetyl bromide 4199-88-6, 5-Nitro-1,10-phenanthroline
12135-76-1, Ammonium **sulfide** 54907-61-8, Iodoacetic anhydride
182087-16-7, GenBank I26206
RL: RCT (Reactant); RACT (Reactant or reagent)
(CAP-phenanthroline **conjugate** for DNA cleavage)
- IT 54258-41-2P, 5-**Amino**-1,10-phenanthroline 111047-29-1P
152572-68-4P 154030-81-6R 182685-66-1P 182685-67-2P 182685-68-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(CAP-phenanthroline **conjugate** for DNA cleavage)

L31 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:328936 CAPLUS

DOCUMENT NUMBER: 122:306484

TITLE: Properties of exonuclease-resistant,
psoralen-conjugated oligodeoxyribonucleotides in vitro
and in cell culture

AUTHOR(S): Levis, Joel T.; Miller, Paul S.

CORPORATE SOURCE: School Hygiene Public Health, Johns Hopkins Univ.,
Baltimore, MD, 21205, USA

SOURCE: Antisense Research and Development (1994), 4(4),
231-41

CODEN: AREDEI; ISSN: 1050-5261

PUBLISHER: Liebert

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have prepared **oligodeoxyribonucleotides** that are
modified at the 3'-terminal with N4-(4-aminobutyl)deoxycytidine
and derivatized at the 5'-end with a 4'-([N-(aminoethyl)**amino**
]methyl)-4,5',8-trimethylpsoralen [(ae)AMT] and whose sequences are
complementary to vesicular stomatitis virus (VSV), N-protein mRNA
[(ae)AMT-II] or VSV M-protein mRNA [(ae)AMT-III]. (Ae)AMT-II cross-links
exclusively to VSV N-mRNA when a mixture of the oligomer and poly(A+) RNA
from VSV-infected cells is irradiated in vitro with long wavelength UV
light at either 20° or 37°. N4-(4-Aminobutyl)deoxycytidine
at the 3'-end of (ae)AMT-II does not appear to affect the binding or
crosslinking of the oligomer to its target RNA. Oligomer (ae)AMT-II is
completely resistant to hydrolysis by the 3'-5'-exonuclease activity found
in fetal calf serum whereas a similar oligomer [(ae)AMT-I] which contains
a 3'-terminal deoxycytidine, is hydrolyzed within 30 min when incubated at
37°. Intact (ae)AMT-II was found in both the cell lysate and cell
culture medium after 12 h of incubation with mouse L-cells along with
d-(ae)AMTpT, which appears to result from endonuclease degradation of the
oligomer. In contrast, no intact (ae)AMT-I was found in either the cell
lysate or the culture medium after 1 h incubation. Although 10 µM
(ae)AMT-II had no effect on VSV-protein synthesis in either unirradiated
or UV-irradiated VSV-infected mouse L-cells, 10 µM (ae) AMT-III
inhibited VSV protein synthesis 30% in irradiated cells. These results
show that introduction of a N4-(4-aminobutyl)deoxycytidine at the 3'-end
of an oligodeoxyribonucleotide significantly increases the resistance of
the oligomer to degradation by 3',5'-exonucleases but does not interfere with
its ability to bind selectively to complementary RNA. Further

derivatization with psoralen creates an oligomer that can be triggered to cross-link with RNA in a sequence-specific manner, is taken up intact by mammalian cells in culture, and exhibits biol. activity. In combination, these two modifications endow the oligodeoxyribonucleotide with novel properties that could be exploited in the design of antisense or antigene reagents for use in controlling gene expression in mammalian cells.

CC 1-12 (Pharmacology)

Section cross-reference(s): 8, 33

IT **Nucleotides**, biological studies

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(oligo-, deoxyribo-, antisense; properties of exonuclease-resistant and psoralen-**conjugated** antisense oligodeoxyribonucleotides in vitro and in cell culture in relation to vesicular stomatitis virus **protein synthesis inhibition**).

L31 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:625876 CAPLUS

DOCUMENT NUMBER: 121:225876

TITLE: Preparation of photoprotein **conjugates** and methods of use thereof

INVENTOR(S): Stults, Nancy L.

PATENT ASSIGNEE(S): Sealite Sciences, Inc., USA

SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9418342	A1	19940818	WO 1994-US1387	19940204
W:	AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN			
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9461718	A1	19940829	AU 1994-61718	19940204
EP 683822	A1	19951129	EP 1994-908734	19940204
EP 683822	B1	20020502		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE			
JP 08506897	T2	19960723	JP 1994-518303	19940204
AT 217086	E	20020515	AT 1994-908734	19940204
IL 108607	A1	19981206	IL 1994-108607	19940209
PRIORITY APPLN. INFO.:			US 1993-17116	A 19930212
			WO 1994-US1387	W 19940204

AB The present invention encompasses a method of synthesis of **conjugates** of photoproteins that retain all or a substantial portion of the luminescent activity of underivatized photoprotein. According to the present invention photoproteins may be **conjugated** with a variety of binding reagents including streptavidin/avidin, glycoproteins, lectins, hormones, antigens, drugs, antibodies and antigen binding fragments thereof, or any other selectively bindable reagent by chemical **crosslinking** means. The present invention also encompasses **conjugates** produced by this method, and methods of use of such **conjugates**. Aequorin was activated with 2-iminothiolane and then **conjugated** with **sulfo-MCC**-activated monoclonal antibody to human TSH. The

conjugate was used in an immunoassay for TSH.

IC ICM C12Q001-00
ICS C12Q001-66

CC 9-14 (Biochemical Methods)
Section cross-reference(s): 2

ST photoprotein **conjugate** binding reagent prepn; aequorin antibody
conjugation TSH immunoassay

IT Ostracoda
Pelagia
(binding reagents **conjugates** with bioluminescent
proteins of)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
(Analytical study); PREP (Preparation); USES (Uses)
(bioluminescent, **conjugates** with binding reagents;
photoprotein **conjugates** preparation and use as reagents in
luminescence binding assays).

IT Aequorins
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
(Analytical study); PREP (Preparation); USES (Uses)
(**conjugates** with binding reagents; photoprotein
conjugates preparation and use as reagents in luminescence binding
assays)

IT Pharmaceuticals
(**conjugates** with photoproteins; photoprotein
conjugates preparation and use as reagents in luminescence binding
assays)

IT Agglutinins and Lectins
Antibodies
Antigens
Hormones
Ligands
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
(Analytical study); PREP (Preparation); USES (Uses)
(**conjugates** with photoproteins; photoprotein
conjugates preparation and use as reagents in luminescence binding
assays)

IT Immunoassay
Nucleic acid hybridization
(photoprotein **conjugates** preparation and use as reagents in
luminescence binding assays)

IT Aequorins
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
(Analytical study); PREP (Preparation); USES (Uses)
(apo-, **conjugates** with binding reagents; photoprotein
conjugates preparation and use as reagents in luminescence binding
assays)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
(Analytical study); PREP (Preparation); USES (Uses)
(berovins, apo-, **conjugates** with binding reagents;
photoprotein **conjugates** preparation and use as reagents in
luminescence binding assays)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
(Analytical study); PREP (Preparation); USES (Uses)
(berovins, **conjugates** with binding reagents; photoprotein
conjugates preparation and use as reagents in luminescence binding
assays)

IT Avidins

Deoxyribonucleic acids

Enzymes

Glycoproteins, specific or class

Nucleic acids

Peptides, preparation

Receptors

Ribonucleic acids

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(**conjugates**, * luminescence **binding** assays

Deoxyribonucleic acSESEnzymesMROLES ASStGlycoproteins, speccesNucleic acids R6Peptides, preparatiD IReceptors ROLES)

IT Spectrochemical analysis

(luminescence, photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Proteins**, specific or class

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(mnemiopsins, apo-, **conjugates** with binding reagents;

photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Proteins**, specific or class

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(mnemiopsins, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Proteins**, specific or class

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(obelins, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Proteins**, specific or class

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(obelins, apo-, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Nucleotides**, preparation

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(oligo-, **conjugates**, with photoproteins; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Proteins**, specific or class

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(photo-, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT 51-48-9, Thyroxine, analysis 9002-71-5, TSH

RL: ANT (Analyte); ANST (Analytical study)

(photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT 51-48-9D, Thyroxine, aequorin **conjugates**

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)

(photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT 9013-20-1DP, Streptavidin, **conjugates** with photoprotein

9014-00-ODP, Luciferase, **conjugates** with binding reagents
 96827-88-2DP, Pholasin, **conjugates** with binding reagents
 RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
 (Analytical study); PREP (Preparation); USES (Uses)
 (photoprotein **conjugates** preparation and use as reagents in
 luminescence binding assays)

IT 4856-87-5 6539-14-6, 2-Iminothiolane 6953-60-2, S-
 Acetylmercaptosuccinic anhydride 7803-49-8, Hydroxylamine, reactions
 15209-14-0, Bis(maleimido) methyl ether 42014-51-7 55750-63-5
 58626-38-3 58626-38-3D, sulfonated 64987-85-5, SMCC 68181-17-9,
 N-Succinimidyl-3-(2-pyridyldithio)propionate 72252-96-1 72252-96-1D,
 sulfonated 76931-93-6 79886-55-8 79886-55-8D, sulfonated
 103708-09-4 112241-19-7
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (photoprotein **conjugates** preparation and use as reagents in
 luminescence binding assays)

L31 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:184685 CAPLUS
 DOCUMENT NUMBER: 120:184685
 TITLE: Oligonucleotides having conjugates attached at the
 2'-position of the sugar moiety
 INVENTOR(S): Cook, Alan Frederick; Rao, Kambhampati Venkata Babaji
 PATENT ASSIGNEE(S): Pharmagenics, Inc., USA
 SOURCE: PCT Int. Appl., 39 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9323570	A1	19931125	WO 1993-US4144	19930428

W: CA, JP

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1992-881255 19920511

AB An oligonucleotide wherein at least one nucleotide unit thereof is
 substituted at the 2'" position with a moiety -(L)n-R1, wherein L is a
 linker group, and n is 0 or 1; R1 is a moiety which improves uptake of the
 oligonucleotide into the cell and/or increases the stability of the
 oligonucleotide. The oligonucleotides may be employed for binding to an
 RNA, a DNA, a protein, or a peptide to inhibit or prevent gene
 transcription or gene expression, to inhibit or stimulate the activities
 of target mols., or the oligonucleotides may be employed as diagnostic
 probes for determining the presence of specific DNA or RNA sequences or
 proteins. Thus, glucose-attached modified oligonucleotide AGTGTTCAGTTCCGU
 was prepared through multiple steps by using S-Et trifluorothioacetate and
 2,2'-anhydro-1-(β -D-arabinofuranosyl)uracilas starting material.

IC ICM C12Q001-68

ICS A61K031-70; C07H021-02

CC 3-6 (Biochemical Genetics)

Section cross-reference(s): 1, 9, 33

IT Amino acids

Carbohydrates

Dipeptides

Hormones, animal

Neurotransmitters

Peptides

Proteins

Steroids
Sterols
Vitamins

RL: RCT (Reactant); RACT (Reactant or reagent)

(oligonucleotide modified with, for binding
DNA, RNA, peptide and protein)

IT 51989-21-0 118849-17-5 153143-74-9 153143-74-9D, conjugates
with long chain aminoalkylcontrolled pore glass 153835-23-5
153835-24-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of sugar-attached
oligonucleotide, for binding to RNA or DNA or
protein)

L31 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:2234 CAPLUS

DOCUMENT NUMBER: 120:2234

TITLE: Modified oligonucleotides for recognition and cleavage
of RNA and their use in disease treatment

INVENTOR(S): Cook, Phillip Dan; Bruice, Thomas; Guinosso, Charles
John; Kawasaki, Andrew Mamoru; Griffey, Richard

PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 119 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 110

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9317717	A1	19930916	WO 1993-US2057	19930305
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 5359051	A	19941025	US 1992-846556	19920305
US 5514786	A	19960507	US 1992-942961	19920910
AU 9337944	A1	19931005	AU 1993-37944	19930305
JP 07502749	T2	19950323	JP 1993-515946	19930305
EP 656790	A1	19950614	EP 1993-907292	19930305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 6358931	B1	20020319	US 1994-295744	19940830
AU 713740	B2	19991209	AU 1997-26244	19970624
AU 9726244	A1	19971106		
US 6232463	B1	20010515	US 1998-128508	19980804
US 2002160972	A1	20021031	US 2001-974326	20011010
US 6610663	B2	20030826		

PRIORITY APPLN. INFO.:

US 1992-846556	A	19920305
US 1992-942961	A2	19920910
US 1990-463358	B2	19900111
US 1990-566977	B2	19900813
WO 1991-US243	A2	19910111
AU 1993-38025	A3	19930225
WO 1993-US2057	A	19930305
US 1994-295744	A3	19940830
US 1997-948151	A1	19971009

AB The title modified oligonucleotides comprise an RNA cleaving moiety having
at least general acid/base properties linked via an aryl or heteroaryl
moiety to the oligonucleotide. The aryl or heteroaryl moiety may be an...

intercalating group such as phenanthrene. The RNA cleaving moiety may be a (substituted) imidazole or bis-imidazole, or may be a structure which binds 1 or 2 metal ions. The oligonucleotide is preferably modified at the 2' hydroxyl of the sugar. The synthesis of a representative modified nucleoside, 9-((4-(7-(-5-imidazolyl-1-H)naphthyl)-O-2-propyloxy-)b-D-ribofuranosyl))adenine, was presented. This nucleoside may be incorporated into an antisense oligonucleotide to prepare a modified oligonucleotide of the invention. Methods for screening of candidate modified oligonucleotides for specificity, nuclease resistance, and RNA cleavage activity are described.

IC ICM A61K048-00

ICS C12Q001-68

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 1, 33

IT Disease

(caused by pathol. production of **protein**, treatment of, antisense **oligonucleotide conjugates** with intercalating agent and RNA-cleaving moiety for)

IT **Proteins**, biological studies

RL: PREP (Preparation)

(production of, patholog., treatment of, antisense **oligonucleotide conjugates** with intercalating agent and RNA-cleaving moiety for)

IT 58-61-7, Adenosine, reactions 106-96-7, Propargyl bromide 109-94-4, Ethyl formate 358-23-6, Trifluoromethanesulfonic anhydride 582-17-2, 2,7-Naphthalenediol 1461-22-9, Tributyltin chloride 2450-71-7, Propargyl **amine** 2537-48-6, Diethylcyanomethylphosphonate 3587-60-8, Benzylchloromethyl ether 5425-44-5, 2-Phenyl-1,3-dithiane 13528-93-3 16703-52-9, Ethyl N,N-dimethyl oxamate 18162-48-6, t-Butyldimethylchlorosilane 40615-36-9 69304-37-6, 1,3-Dichlorotetraisopropyl disiloxane 129378-52-5

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, in preparation of **modified** nucleoside for RNA-cleaving antisense **oligonucleotides**)

L31 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1992:444063 CAPLUS

DOCUMENT NUMBER: 117:44063

TITLE: Antibodies to ligand analogs and their utility in ligand-receptor assays

INVENTOR(S): Valkirs, Gunars Edwin; Buechler, Kenneth Francis

PATENT ASSIGNEE(S): Biosite Diagnostics, Inc., USA

SOURCE: Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 475783	A1	19920318	EP 1991-308408	19910913
EP 475783	B1	19991201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5143852	A	19920901	US 1990-583046	19900914
CA 2071904	AA	19920315	CA 1991-2071904	19910904
CA 2071904	C	20030218		
WO 9205283	A1	19920402	WO 1991-US6325	19910904
W: AU, CA, FI, JP, NO				
AU 9185361	A1	19920415	AU 1991-85361	19910904

JP 05501922	T2	19930408	JP 1991-515353	19910904
AT 187250	E	19991215	AT 1991-308408	19910913
ES 2141086	T3	20000316	ES 1991-308408	19910913
FI 9202145	A	19920512	FI 1992-2145	19920512
NO 9201864	A	19920714	NO 1992-1864	19920512
PRIORITY APPLN. INFO.:			US 1990-583046	A 19900914
			WO 1991-US6325	A 19910904

AB A competitive ligand-receptor assay uses an antibody to a ligand analog which has substantially (e.g. >100-fold) greater affinity for the ligand analog than for the target ligand. The target ligand is determined in a fluid sample by (a) contacting the sample with a ligand receptor and a ligand analog **conjugated** to a signal-generating label, such that the amount of ligand analog **conjugate** not bound to the receptor is related to the concentration of the target ligand in the sample; (b) contacting the fluid with ≥ 1 ligand analog antibody, so that an amount of ligand analog **conjugate** not bound to the ligand receptor is bound by the antibody; (c) contacting the fluid with a receptor capable of binding to the ligand analog antibody; (d) removing the ligand analog antibody bound to this receptor from the fluid; (e) detecting the ligand analog **conjugate** bound to the ligand analog antibody; and (f) relating the signal to the presence of amount of the target ligand in the sample. Alternative embodiments of the assay, and test devices for performing the assay, are claimed. Thus, for an assay for benzoylecgonine (I), the reaction product (II) of p-acetylthiopropionamide benzoylecgonine with sulfosuccinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate and aminoethanesulfonic acid was prepared and **conjugated** to alkaline phosphatase; this **conjugate** (III) was used as ligand analog **conjugate** in the assay. A sample containing I was incubated with III and a membrane-immobilized monoclonal antibody to II; the membrane was then washed and incubated with 3-indoxyl phosphate to generate a blue color in the presence of bound III. Multiple stds. were used to establish the assay response as a function of I concentration

IC ICM G01N033-53
ICS G01N033-543; G01N033-541

CC 9-10 (Biochemical Methods)

IT Deoxyribonucleic acids

RL: ANT (Analyte); ANST (Analytical study)
(determination of, by receptor binding assay, antibody to **DNA** analog in)

IT **Proteins**, analysis

RL: ANT (Analyte); ANST (Analytical study)
(determination of, by receptor binding assay, antibody to **protein** analog in)

IT Albumins, compounds
Hemocyanins

Proteins, specific or class

RL: SPN (Synthetic preparation); PREP (Preparation)
(**conjugates**, with benzoylecgonine analog, preparation of, for benzoylecgonine immunoassay)

IT 142209-49-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reaction with **proteins**)

IT 9001-78-9DP, Alkaline phosphatase, **conjugates** with benzoylecgonine analog

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for benzoylecgonine immunoassay)

IT 103708-09-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with aminoethanesulfonic acid and benzoylecgonine analog,

for benzoylecgonine immunoassay)

IT 107-35-7

RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with benzoylecgonine analog and **linking agent**,
 for benzoylecgonine immunoassay)

IT 64987-85-5D, **protein conjugates 103708-09-4D**
, protein conjugates

RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with benzoylecgonine derivative)

L31 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1991:466230 CAPLUS

DOCUMENT NUMBER: 115:66230

TITLE: Method for coupling oligonucleotide probes with proteins

INVENTOR(S): Garman, Andrew John

PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK

SOURCE: Eur. Pat. Appl., 16 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 422861	A2	19910417	EP 1990-310985	19901008
EP 422861	A3	19910925		
EP 422861	B1	20000517		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 193019	E	20000615	AT 1990-310985	19901008
JP 03290200	A2	19911219	JP 1990-277613	19901015
JP 3015445	B2	20000306		
US 5800985	A	19980901	US 1994-310057	19940922
PRIORITY APPLN. INFO.:			GB 1989-23089	A 19891013
			GB 1989-24822	A 19891103
			US 1990-596302	B1 19901015

OTHER SOURCE(S): MARPAT 115:66230

AB Protein-labeled DNA, RNA, or **oligonucleotides** probes

are prepared by (1) reacting the protein with a heterobifunctional linker which ~~introduces a thiol-reactive group into the protein~~ (e.g.

succinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate; (2)

introducing an **amino** group-containing linker into the probe, e.g.

with a reagent such as **amino** link 1; (3) reacting the probe

derivative with a thiolating agent such as Traut's reagent or homocysteine

lactone to introduce a **thiol** group; and (4) reacting the protein

derivative of step 1 with the probe derivative of step 3. The probes are

easily

made and offer an economic alternative to conventional radiolabeled probes. Alkaline phosphatase and horseradish peroxidase-labeled hybridization probes were prepared by the described procedure and used in hybridization assays.

IC ICM C07H021-00

ICS C12Q001-68

CC 3-5 (Biochemical Genetics)

ST DNA RNA oligonucleotide protein

conjugate; hybridization probe protein labeling

IT Nucleotides, polymers

RL: PREP (Preparation)

(oligo-, **conjugates**, with **proteins**, preparation of,

simple method for)

IT **Nucleotides**, polymers

RL: PREP (Preparation)

(oligo-, deoxyribo-, **conjugates**, with **proteins**,
preparation of, simple method for)

IT 1195-16-0, N-Acetylhomocysteine thiolactone 6539-14-6, 2-Iminothiolane
10593-85-8, Homocysteine thiolactone

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with **amino group-containing oligonucleotide**
derivative, protein-labeled hybridization probe preparation in relation to)

L31 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1991:38819 CAPLUS

DOCUMENT NUMBER: 114:38819

TITLE: Preparation of covalent conjugates of
oligodeoxynucleotides and poly(amino acids) or
proteins

INVENTOR(S): Westermann, Peter; Gross, Burckhard; Hoinkis, Guenter

PATENT ASSIGNEE(S): Akademie der Wissenschaften der DDR, Ger. Dem. Rep.

SOURCE: Ger. (East), 5 pp.

CODEN: GEXXA8

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 273445	A1	19891115	DD 1988-317326	19880629
PRIORITY APPLN. INFO.:			DD 1988-317326	19880629
OTHER SOURCE(S):	MARPAT	114:38819		

AB The title conjugates are prepared by synthesizing an
oligodeoxyribonucleotide on a carrier-bound spacer
-CONH(CH₂)_nO₂C(CH₂)₂CONH(CH₂)nOH (n = 2-6) by the phosphoramidite method,
cleaving from the carrier to provide a 3'-carboxy-**modified**
oligonucleotide X-3'-OP(O)(O-)O(CH₂)_nNHCO(CH₂)₂CO₂H (X =
oligonucleotide), activating the carboxy group with e.g.
1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, and condensing the product
with a poly(**amino acid**) or protein. The conjugate, containing an
antisense oligonucleotide complementary to a cellular or viral gene,
inhibits expression of the corresponding gene in cells by hybridizing with
the gene. Thus, a conjugate of 5'-CCTCACTACTTCTGGAATAGC-3' with
poly-L-lysine inhibited expression of the T-antigen gene of SV40 virus in
COS cells at 5-20 μM.

IC ICM C07H021-04

ICS C07K013-00; C07K015-00

CC 9-14 (Biochemical Methods)

Section cross-reference(s): 1

ST gene expression **oligonucleotide protein**
conjugate

IT **Nucleotides**, polymers

RL: ANST (Analytical study)

(oligo-, deoxy-, **conjugates**, with poly(amino acids) and
proteins, gene expression inhibition by)

L31 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1991:20608 CAPLUS

DOCUMENT NUMBER: 114:20608

TITLE: Molecular sticks for controlling **protein**
conformation

INVENTOR(S): Kauvar, Lawrence M.
 PATENT ASSIGNEE(S): Terrapin Diagnostics, Inc., USA
 SOURCE: RCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8909233	A1	19891005	WO 1989-US1195	19890323
W: AU, BR, DK, FI, HU, JP, KR, NO, RO, SU				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8934395	A1	19891016	AU 1989-34395	19890323
PRIORITY APPLN. INFO.:			US 1988-172623	19880324
			WO 1989-US1195	19890323

GI

Cys-Ala-Asp-Pro-Tyr-Glu-Glu-Gly-Asp-Asp-Gly-Arg-Thr-Cys I

AB Methods of stabilizing 3-dimensional conformations of proteins using mol. sticks are provided. A method for controlling conformation of a target peptide in solution comprises (1) providing a pair of 1st **linking** groups at designated points in the sequence of the target peptide; and (2) **conjugating** the **linking** groups to a mol. stick containing, at each and of the spacer portion thereof, a pair of 2nd **linking** groups compatible with the 1st **linking** groups. The rigid multimeric portions of the mol. sticks may be of various lengths. Proteins or peptides thus stabilized are useful in diagnosis and therapy, especially under conditions where unstabilized proteins would be denatured. Thus, mol. sticks of varying length were prepared from extension of primed oligonucleotides with Escherichia coli polymerase I and a mixture of nucleotides in which the thymidine triphosphate was derivatized to the sulfo-M-maleimido-benzoylsulfosuccinimide (**sulfo-MBS**) ester; the MBS-derivatized thymidine was capable of further reaction with sulfhydryl groups to provide thioether **linkages** to a target peptide. The peptide I, and monoclonal antibodies (MAbs) against it, were prepared with standard techniques. Samples of the peptide were reacted with the

mol. sticks (Liu et al., 1979) and the restricted peptides tested for affinity to the MAb. The I50 (concentration of tethered peptide at which peptide binding is inhibited by 50%) is then plotted.

IC ICM C07K015-00

ICS C07K017-06; C07H015-12

CC 9-2 (Biochemical Methods)

Section cross-reference(s): 6

ST mol stick peptide **protein** stabilization; **nucleotide**

mol stick peptide stabilization

IT Peptides, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(**crosslinking** with mol. sticks, stability of conformation in relation to)

IT Stabilizing agents

(for peptide and **protein** conformation, mol. sticks for)

IT **Crosslinking** agents

- (in mol. sticks for peptides)
- IT Pharmaceuticals
Vaccines
(mimotope of, mol. sticks for **crosslinking**, stability of conformation in relation to)
- IT **Proteins**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(mol. sticks for **crosslinking**, stability of conformation in relation to)
- IT Amino acids, biological studies
Nucleotides, biological studies
RL: BIOL (Biological study)
(mol. sticks of, for stabilization of peptide conformation)
- IT Mercapto group
(of peptide, mol. stick **linker** binding to)
- IT Conformation and Conformers
(stabilization of, of peptides and **proteins**, mol. sticks for)
- IT **Crosslinking** agents
(heterobifunctional, of mol. stick for stabilization of peptide conformation)
- IT 365-08-2D, Thymidine triphosphate, sulfomaleimidobenzoylsulfosuccinimide esters 131060-22-5D, thymidine triphosphate derivs.
RL: ANST (Analytical study)
(in preparation of **oligonucleotide** mol. sticks for peptide stabilization)

L31 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1990:511968 CAPLUS
 DOCUMENT NUMBER: 113:111968
 TITLE: Methods, supports, and kits for multiple target analyses through nucleic acid hybridization
 INVENTOR(S): Adams, Trevor H.; Schwartz, Dennis E.; Vermeulen, Nicolaas M. J.; Petrie, Charles R.
 PATENT ASSIGNEE(S): Microprobe Corp., USA
 SOURCE: PCT Int. Appl., 80 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9001564	A1	19900222	WO 1989-US3378	19890807
W: JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
PRIORITY APPLN. INFO.:		US 1988-230066	19880809	
		US 1989-388202	19890804	

AB Hybridization assays are provided wherein a multiplicity of different nucleic acid probes for the site-specific capture of target nucleic acids are **conjugated** to specific locations upon a single dipstick or device. The use of a dipstick has substantial mech. advantages over prior art formats for nucleic acid hybridizations. The dipsticks are composed of a handle and a nonporous support coated with a solid surface having ≥ 1 discrete region of nucleic acids covalently bound thereto. Also provided are means for covalently attaching nucleic acids to solid supports, improved hybridization buffers, improved support surfaces, methods for reducing nonspecific background, and methods for quantifying assay results. A multiple target dipstick for the detection of specific bacteria in patient plaque samples was prepared by immobilizing 24-mer

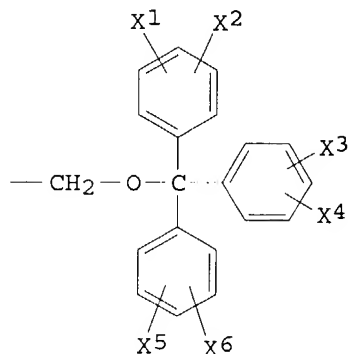
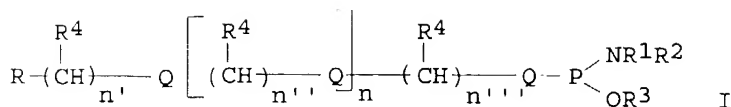
nucleotide species-specific sequences complementary to the hypervariable region of the 16S rRNAs from *Actinobacillus actinomycetemcomitans*, *Bacteroides gingivalis*, *Eikenella corrodens*, and *Bacteroides intermedius* in different slots on a Pall membrane derivatized with 2-aminoethanethiol. The 24-mers were synthesized possessing a 5'-terminal amine hexyl **linker**. The dipstick was placed in a sonicated solution containing lysing buffer and plaque sample, it was contacted with a solution containing biotinylated oligonucleotide universal sequence probes, and the filter was washed, reacted with streptavidin-peroxidase **conjugate**, and developed. One or all of the bacteria could be detected in a complex mixture of cells and organic material.

- IC ICM C12Q001-68
- CC 9-2 (Biochemical Methods)
Section cross-reference(s): 33
- IT Latex
(**conjugates** with nucleic acid probes, for multiple target nucleic acid hybridization assays)
- IT Immobilization, biochemical
(of nucleic acids and **proteins** on dipstick for nucleic acid hybridization assays)
- IT Metals, uses and miscellaneous
RL: USES (Uses)
(on solid support for nucleic acid hybridization assay, disulfide and thiol ester **linkages** in relation to)
- IT Glass, oxide
RL: ANST (Analytical study)
(**conjugates**, with nucleic acid probes, for multiple target nucleic acid hybridization assays)
- IT Albumins, compounds
Caseins, compounds
Gelatin, compounds
Proteins, specific or class
RL: ANST (Analytical study)
(**conjugates**, with sulfhydryl group-containing polymer, on nucleic acid hybridization assay dipstick)
- IT Coating materials
(hydrophilic, on solid support for nucleic acid hybridization assay, disulfide and thiol ester **linkages** in relation to)
- IT Coating materials
(hydrophobic, on solid support for nucleic acid hybridization assay, disulfide and thiol ester **linkages** in relation to)
- IT **Nucleotides**, polymers
RL: ANST (Analytical study)
(oligo-, **conjugates**, with dipstick for multiple target assay)
- IT 9002-84-0D, Teflon, carboxyl group-modified, nucleic acid probe
conjugates 9003-53-6D, Polystyrene, nucleic acid probe
conjugates 108317-04-0D, Nytran, nucleic acid probe
conjugates
RL: ANST (Analytical study)
(for multiple target nucleic acid hybridization assays)
- IT 126601-23-8D, amine hexyl **linker** derivs., membrane
conjugates 126601-36-3 128768-66-1 128768-67-2
RL: ANST (Analytical study)
(multiple target nucleic acid hybridization assay dipstick containing, for periodontal disease bacteria detection)
- IT 60-23-1DP, 2-Aminoethanethiol, membrane **conjugates**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with modified **oligonucleotides** in preparation of hybridization dipstick)

IT 106145-13-5DP, oligonucleotide probe and membrane
 reaction products 128768-74-1DP, membrane **conjugates**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, for hybridization assays)

L31..ANSWER.33 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN.
 ACCESSION NUMBER: 1990:139562 CAPLUS
 DOCUMENT NUMBER: 112:139562
 TITLE: Phosphoramidite reagents for functionalizing
oligonucleotides with **amine**
 ,hydroxyl, or **thiol** groups
 INVENTOR(S): Levenson, Corey; Chang, Chu An; Oakes, Fred T.
 PATENT ASSIGNEE(S): Cetus Corp., USA
 SOURCE: PCT Int. Appl., 48 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8902931	A1	19890406	WO 1988-US3212	19880919
W: DK, FI, JP, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4914210	A	19900403	US 1987-104200	19871002
EP 380559	A1	19900808	EP 1988-908841	19880919
EP 380559	B1	19931222		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 03501383	T2	19910328	JP 1988-508099	19880919
AT 98996	E	19940115	AT 1988-908841	19880919
CA 1310600	A1	19921124	CA 1988-578519	19880927
IL 87879	A1	19930610	IL 1988-87879	19880929
PRIORITY APPLN. INFO.:			US 1987-104200	19871002
			EP 1988-908841	19880919
			WO 1988-US3212	19880919
OTHER SOURCE(S):		MARPAT 112:139562		
GI				



II

AB Phosphoramidite reagents [I; R¹, R² = H, lower alkyl; R³ = β-cyanoethyl, methyl; R = protected or unprotected **amino**, **sulphydryl**, or hydroxyl moiety; R⁴ = H, CH₂OH or II (X₁-X₆ = H, lower alkyl, lower alkoxy); Q = O, NH, etc.; n, n', n'', n''' are integers] have a hydrophilic spacer arm and are suitable for introducing functional groups onto **oligonucleotides**. The reagents are more convenient to use than those of the prior art. Their synthesis and uses are described. An oligonucleotide was coupled with a tritylthio polyether phosphoramidite under standard phosphoramidite coupling procedures to yield a tritylthio oligomer. After detritylation of the oligomer it was incubated with N-maleimido-6-aminocaproyl 4-hydroxy-3-nitrobenzene **sulfonate**-derivatized horseradish peroxidase at 4 °C for 2 days. Unreacted starting materials were separated from the end-products by chromatog. The conjugate was detectable by coincidence of peaks of absorbance at 260 nm and 402 nm (heme group of peroxidase).

IC ICM C12Q001-68

ICS C07F009-24

CC 29-7 (Organometallic and Organometalloidal Compounds)

Section cross-reference(s): 33, 37

ST **oligonucleotide protein conjugate**;

amino group contg phosphoramidite **oligonucleotide**

derivs; **hydroxy** group contg phosphoramidite **oligonucleotide**

derivs; **thiol** group contg phosphoramidite

oligonucleotide derivs

IT **Amino**-group

Mercapto group

(**oligonucleotides** containing, preparation of, phosphoramidite functionalizing reagents for)

IT **Nucleotides**, polymers

RL: RCT (Reactant); RACT (Reactant or reagent)

(oligo-, phosphoramidite reagents for derivatization of, **amino** or **thiol** or hydroxy group containing)

IT 9003-99-ODP, Peroxidase, reaction products with

maleimidoaminocaproylhydroxynitrobenzene **sulfonate**

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

L31 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:614504 CAPLUS
 DOCUMENT NUMBER: 107:214504
 TITLE: Radioactive labeling of proteins with nucleosides or nucleotides
 INVENTOR(S): Dattagupta, Nanibhushan
 PATENT ASSIGNEE(S): Molecular Diagnostics, Inc., USA
 SOURCE: U.S., 3 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4692509	A	19870908	US 1984-675373	19841127

PRIORITY APPLN. INFO.: US 1984-675373 19841127

AB A radioactively labeled protein is prepared by covalently linking the protein (e.g. insulin, Ig, protein A) to a radioactive nucleoside or nucleotide through an NH₂ group of the protein and a carbonyl group of a ring-opened sugar moiety of the nucleoside or nucleotide. The labels can be used to indicate the presence and amount of the protein in a biol. assay. ¹⁴C-labeled ATP was oxidized by treatment with NaIO₄ at room temperature for 30 min. The oxidized nucleoside phosphate was adjusted to pH 8 and incubated with anti-Ig antibody for 1 h. The Schiff's base-containing product was then reduced with aqueous NaBH₄. Immobilized native DNA was incubated with diluted serum samples for 1 h, washed, incubated with the labeled antibody for 1 h, and washed. The mixture was irradiated with 260 nm light in the presence of 1% SDS for 30 min to release bound DNA in solution, and the radioactivity of the mixture was counted after adding scintillation fluid. Radioactivity associated with the beads before photodecompn. or in solution after photodecompn. indicates the presence of anti-double-stranded DNA antibody and thus the presence of systemic lupus erythematosus.

IC ICM A61K043-00
ICS A61N005-12

NCL 530303000

CC 9-10 (Biochemical Methods)
Section cross-reference(s): 8, 15

ST radiolabel nucleotide nucleoside protein conjugate; systemic lupus erythematosus RIA; Ig radiolabel oxidized ATP

IT Proteins, specific or class
RL: ANST (Analytical study)
(A, conjugates, with radiolabeled nucleotides or nucleosides, for bioassays)

IT Immunoglobulins
Proteins, specific or class
RL: ANST (Analytical study)
(conjugates, with radiolabeled nucleotides or nucleosides, for bioassays)

IT Nucleosides, compounds
Nucleotides, compounds
RL: ANST (Analytical study)
(labeled, conjugates, with proteins, for bioassays)

IT 7439-97-6D, Mercury, radioisotopes, uses and miscellaneous 7440-44-0D, Carbon, radioisotopes, uses and miscellaneous 7553-56-2D, Iodine, radioisotopes, uses and miscellaneous 7704-34-9D, Sulfur, radioisotopes, uses and miscellaneous 7723-14-0D, Phosphorus, radioisotopes, uses and miscellaneous 10028-17-8, uses and miscellaneous

Ceperley 10/032,592

RL: USES (Uses)
(nucleotides and nucleosides labeled with, for labeling proteins)

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